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# Developing Earth-Abundant Metal-Catalysts for Hydrofunctionalisation

James Paliga



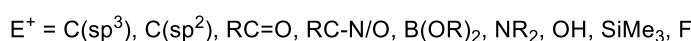
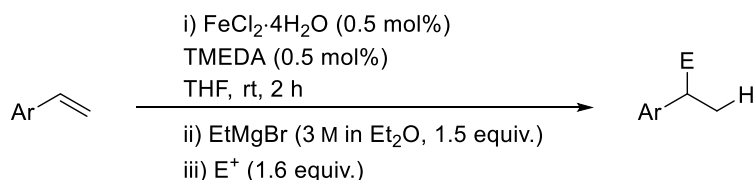
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A thesis submitted for the degree of  
Doctor of Philosophy

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## Abstract

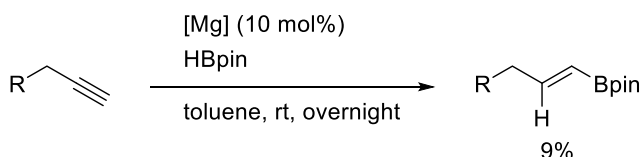
The iron-catalysed hydromagnesiation of styrene derivatives has been developed further from previous publications, expanding the electrophile scope to enable the regioselective formation of new carbon-carbon and carbon-heteroatom bonds (Scheme A1). A commercially available pre-catalyst and ligand were used to give an operationally simple procedure that did not require prior synthesis of a catalyst. This work also investigated the hydromagnesiation of dienes, using a screen of ligands commonly used in transition metal catalysis.



**Commercially available starting materials**  
**Operationally simple, one-pot procedure**

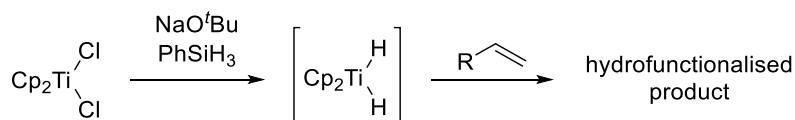
**Scheme A1:** Iron-catalysed hydrofunctionalisation via an *in-situ* generated reactive intermediate.

An investigation into the magnesium-catalysed hydroboration of olefins was also carried out. Although mostly unsuccessful, it was demonstrated that in the presence of a magnesium catalyst, a small amount of vinyl boronic ester could be formed from an alkyne (Scheme A2). Simple magnesium salts were also investigated for the reduction of carbonyls.



**Scheme A2:** Vinylboronic esters accessed using a magnesium catalyst.

Lastly, this work explored the titanium-catalysed hydrosilylation of olefins, using a novel activation method developed within the group (Scheme A3). The results were compared to those published previously using traditional organometallic activation methods and attempts at identifying conditions to improve chemoselectivity were carried out.



**Scheme A3:** Generation of active titanium species for the hydrofunctionalisation of olefins.

## Lay Summary

The ability to synthesise molecules in a controlled manner is essential for the development of products used in everyday life, such as plastics, fabrics, fertilisers and pharmaceuticals. With ever-growing global chemical demand and energy consumption, the development of efficient, energy saving synthetic processes is of paramount importance. Catalysis offers the single most powerful method that can be used to improve the yield and efficiency of molecular synthesis whilst also reducing waste and energy consumption. Earth-abundant metals, such as iron, magnesium and titanium, make ideal choices as catalysts for future applications.

This work developed novel reactions catalysed by an inexpensive, non-toxic and environmentally-benign iron catalyst. The controlled and efficient synthesis of a range of molecular structures was achieved. Experiments have provided insight into how these reactions work, which should not only provide a greater understanding of the science involved, but also direct future developments towards highly efficient catalysts and catalytic processes. Initial studies investigating the use of magnesium as a catalyst were also carried out and the results are reported within. A novel catalyst activation method previously discovered by the Thomas group was applied to a titanium-catalysed reaction, and compared with similar reactions reported in the literature previously.

## **Declaration**

I certify:

- a) that the thesis has been composed by me, and
- b) either that the work is my own, or, where I have been a member of a research group, that I have made a substantial contribution to the work, such contribution being clearly indicated, and
- c) that the work has not been submitted for any other degree or professional qualification except as specified.

James Paliga

## Acknowledgments

Firstly, I would like to thank my supervisor Stephen Thomas for not only providing advice within the context of chemistry but for his support in general throughout the four years in Edinburgh. I feel as though I have learned much more about chemistry under Steve's supervision than I have throughout the rest of my academic career and there are definitely some chemistry quirks I picked up in the Thomas group that will stay with me for life. Most importantly, Steve has helped shape me into a stronger, more confident and determined person and for that I am truly grateful. I would also like to thank my industry sponsors AstraZeneca and in particular my industrial supervisor Alan Steven for his valuable input over the years, and for his direct supervision during the three months I spent at AstraZeneca, Macclesfield.

The many members of the Thomas group I have worked alongside over the years also require many thanks, as working in Edinburgh wouldn't have been half the pleasure if it wasn't for them. In particular I'd like to thank: Mark for all the time he spent helping me analyse results and coming up with ideas when I began my PhD; Alison for showing me the ropes; Jim for teaching me much about history and chemistry equally and Amy for being a legend. I'd like to thank all the friends I met during my time in Edinburgh, I have many fond memories thanks to all of you.

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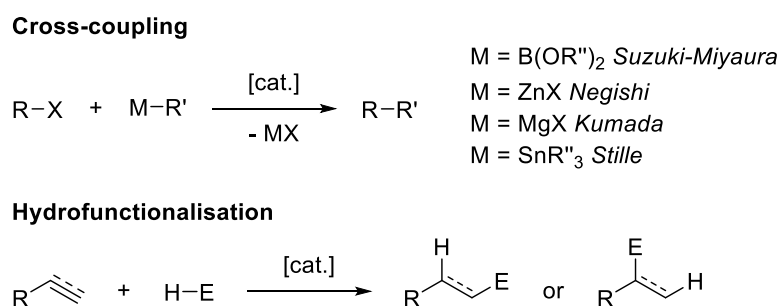
## Abbreviations

Ac	Acetyl
Acac	Acetylacetonate
Alk	Alkyl
Ar	Aryl
BIP	Bisiminopyridine
Bn	Benzyl
Bz	Benzoyl
Bpin	4,4,5,5-Tetramethyl-1,3,2-dioxaborolane
Bu	Butyl
Cp	Cyclopentadienyl
Cy	Cyclohexyl
Dipp	2,6-Diisopropylphenyl
DMF	<i>N,N</i> -Dimethylformamide
EI	Electron ionisation
equiv.	Equivalents
ESI	Electrospray ionisation
Et	Ethyl
GC-MS	Gas chromatography mass spectrometry
Het	Heteroatom
HMDS	Bis(trimethylsilyl)amide
HRMS	High resolution mass spectrometry
<i>J</i>	Coupling constant in Hz
L	Ligand
Ln	Lanthanide
Me	Methyl
Mes	2,4,6-Trimethylphenyl
Naph	Napthalene
NFSI	<i>N</i> -Fluorobenzenesulfonimide
NHC	<i>N</i> -Heterocyclic carbene
NMP	<i>N</i> -Methylpyrrolidine
NMR	Nuclear magnetic resonance
Ph	Phenyl

ppm	Parts per million
Pr	Propyl
R <sub>f</sub>	Retention factor
rt	Room temperature
TEMPO	(2,2,6,6-Tetramethyl-piperidin-1-yl)oxyl
Tf	Trifluoromethanesulfonyl
THF	Tetrahydrofuran
TMEDA	<i>N,N,N',N'</i> -Tetramethylethylenediamine
Ts	<i>para</i> -Toluenesulfonyl
UV	Ultraviolet

## Chapter 1: Introduction

The construction of new carbon-carbon and carbon-heteroatom bonds in a controlled and efficient manner is fundamental to the development of chemical synthesis. In order to efficiently produce new compounds with high chemo-, regio- and stereoselectivity, the modern chemist relies on catalysis. The use of transition metal catalysts is widespread across fine chemical and industrial synthesis to form target compounds, and in particular the use of cross-coupling and hydrofunctionalisation reactions have enabled the use of general methods for the formation of a plethora of new bonds (Scheme 1).<sup>1,2</sup> Hydrofunctionalisation offers an alternative to cross-coupling, where the direct addition of “H-E” across an unsaturated carbon-carbon multiple bond can take place. As olefins provide a synthetically useful functional handle and are generally inert,<sup>3</sup> they can be carried through a synthesis and used to introduce functionality at a late stage. A wide range of functionalised alkenes and alkynes are readily available, reducing the need for complex substrate syntheses prior to the targeted functionalisation.<sup>4</sup>



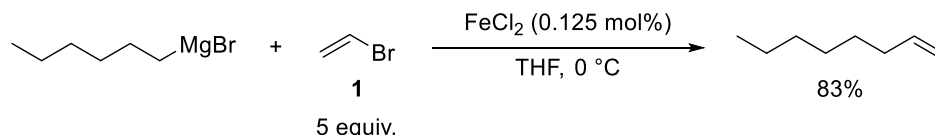
**Scheme 1:** General cross-coupling and hydrofunctionalisation reactions for carbon-carbon and carbon-heteroatom bond forming reactions.

Second- and third-row transition metals, such as palladium, platinum, rhodium and ruthenium, are the most widely adopted metals in catalysis as the well-established two-electron chemistry of these metals, combined with their ease of use and reliability make them very attractive and efficient catalysts.<sup>5</sup> Despite the powerful methodology afforded by these catalysts, the methods inherently suffer from the toxicity and environmental impact of the metals used.<sup>6</sup> Earth-abundant metals are rapidly becoming recognised as alternatives to the more traditionally used transition metals, and there have been numerous reports in the literature detailing the progress in this field.<sup>7</sup>

### 1.1: Iron-Catalysed Cross-Coupling Reactions

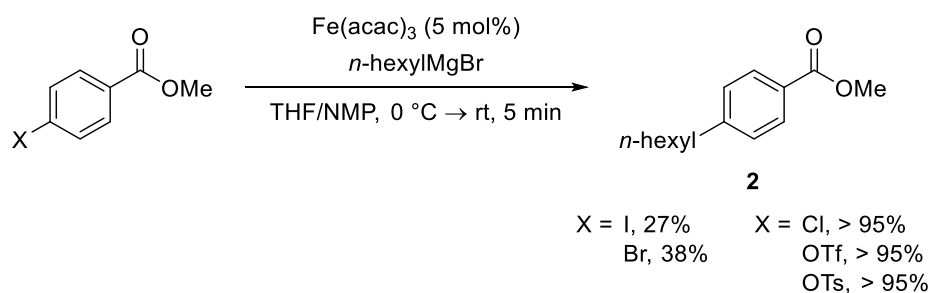
Iron is the most abundant transition metal in the Earth's crust, and as such it has a low cost and long-term commercial availability.<sup>8,9</sup> Although the homo-coupling of aryl Grignard reagents catalysed by iron was

first described by Lichtenwalter in 1939 and then Kharasch in 1941,<sup>10</sup> the field of iron catalysis truly entered the spotlight with the seminal work by Kochi on iron-catalysed cross-coupling of vinyl halides with Grignard reagents (Scheme 2).<sup>11</sup>



**Scheme 2:** Iron-catalysed cross-coupling with vinyl bromide and a Grignard reagent.

Although cross-coupling reactions have since been dominated by precious metal-catalysed reactions, as a general interest in more sustainable chemistry has arisen there has been a great deal of development towards iron-catalysed cross-coupling reactions.<sup>12</sup> One of the practical drawbacks of the work of Kochi was the need for large excesses of the alkenyl halide electrophile **1**. By careful selection of solvent, however, high yields could be obtained using an almost equimolar ratio of Grignard reagent to electrophile. This was first described by Molander, using 1,2-dimethoxyethane for halide-substituted vinylarenes and later a more general system was developed by Cahiez, who reported that a mixture of THF/NMP gave the optimal conditions.<sup>13</sup> It was proposed that the addition of NMP had a stabilising effect on intermediate iron species, preventing possible decomposition pathways, such as  $\beta$ -hydride elimination from the alkyl iron species formed *in situ*. Further development using the same solvent mixture saw the coupling of aryl electrophiles with alkyl Grignard reagents in short reaction times.<sup>14</sup> In addition, the electrophile selectivity was significantly different to previously published cross-coupling methodologies with aryl bromides and iodides giving poor results whereas aryl chlorides, triflates and tosylates gave the product **2** in excellent yields (Scheme 3).

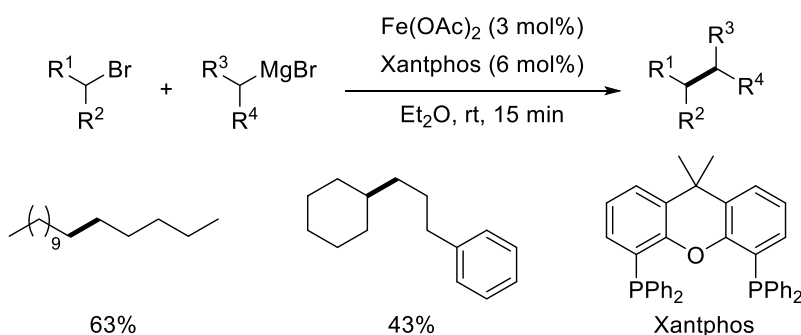


**Scheme 3:** Iron-catalysed cross-coupling of aryl electrophiles with Grignard reagents.

Despite the reports on the homocoupling of aryl Grignard reagents in 1939 and 1941, the first cross-coupling reaction using aryl Grignard reagents was not described until 2002 when Fürstner and Lietner reported the iron-catalysed cross-coupling of heteroaryl electrophiles.<sup>15</sup> In this case, the reaction was carried out solely in THF as the solvent. The drawback of this method, however, was that it was ineffective for

electron-rich electrophiles, which instead led to the homocoupling of the arylmagnesium reagents. By carrying out a transmetallation of the Grignard reagent with CuCN to form the corresponding organocopper species, it was demonstrated that homocoupling could be suppressed and the cross-coupling reaction favoured to give the biaryl products.<sup>16</sup> Further development led to a novel catalyst system using an iron fluoride salt in combination with an *N*-heterocyclic carbene (NHC) ligand that could cross-couple aryl groups bearing dimethylamino, methylthio, fluoro and acetal functionalities.<sup>17</sup>

Significantly, the development of iron-catalysed cross-coupling has now lead to methodologies which enable the formation of new C(sp<sup>3</sup>)-C(sp<sup>3</sup>) bonds. This advance demonstrates a divergence from the reactivity shown by precious metal catalysts,<sup>18</sup> offering additional benefit other than increasing sustainability. The initial investigations into alkyl-alkyl cross-coupling by Kochi revealed that substrates containing β-hydrogens were susceptible to disproportionation, therefore alkyl groups were limited to methyl, neopentyl and benzyl.<sup>19</sup> Extensive screening of various conditions, iron salts and ligands in following reports eventually lead to the discovery of a general coupling of alkyl Grignard reagents and unactivated primary and secondary halides (Scheme 4).<sup>20</sup> The reactions with primary halides proceeded to give the products in a good to moderate yield (46-64%), whereas with secondary halides the yields were generally poorer (8-43%).



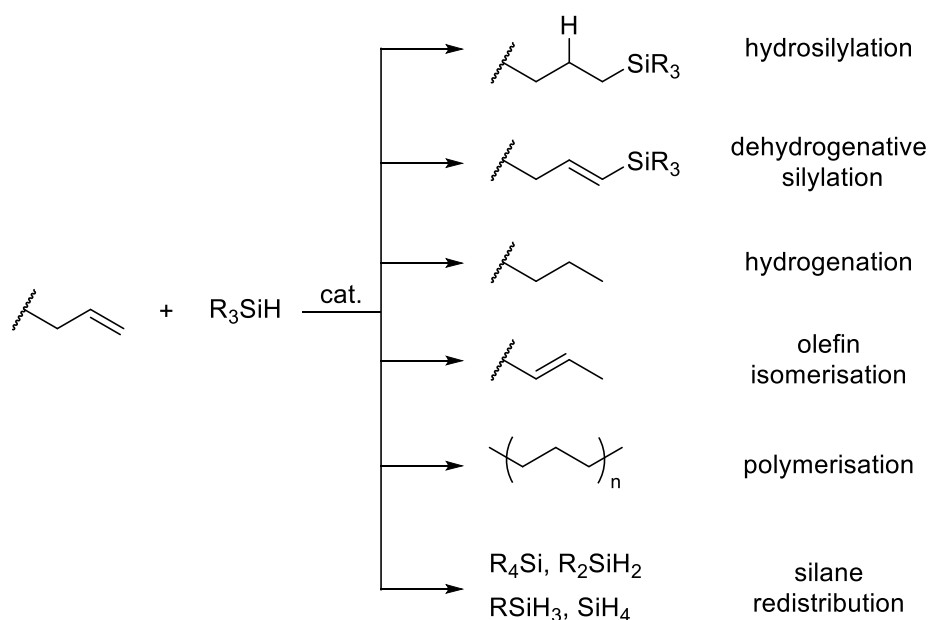
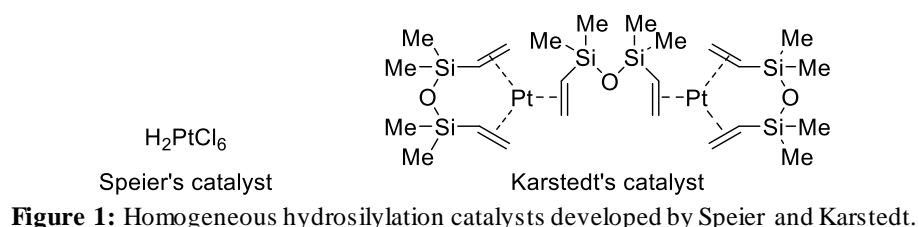
**Scheme 4:** C(sp<sup>3</sup>)-C(sp<sup>3</sup>) cross-coupling catalysed by Fe(OAc)<sub>2</sub> with a bidentate phosphine catalyst.

## 1.2: Iron-Catalysed Hydrofunctionalisation Reactions

For the purpose of this introduction, only the hydrofunctionalisation of olefins using low oxidation-state iron catalysts will be considered. Iron-catalysed hydrofunctionalisation reactions can also be carried out using high oxidation-state catalysts through either Lewis acid or radical mediated reactions,<sup>7g,21</sup> however these are outside the scope of this work.

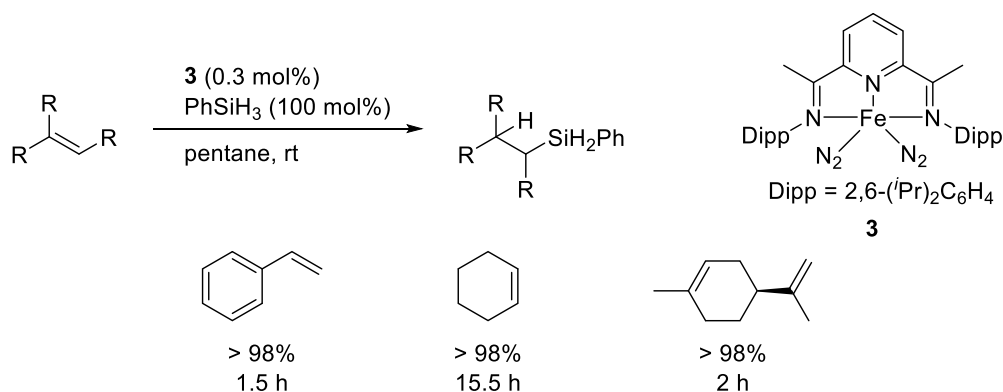
## 1.2.1: Hydrosilylation

Hydrosilylation has become one of the most industrially important processes following the development of Speier's and Karstedt's homogeneous platinum catalysts (Figure 1).<sup>22,23</sup> The products of olefin hydrosilylation are used in a vast number of applications in both materials and fine chemical synthesis.<sup>24,25</sup> Until recently, hydrosilylation has been dominated by the use of precious metal catalysts, typically platinum and rhodium complexes although these complexes are susceptible to dehydrogenative silylation amongst other side reactions (Scheme 5).<sup>24a,26</sup>



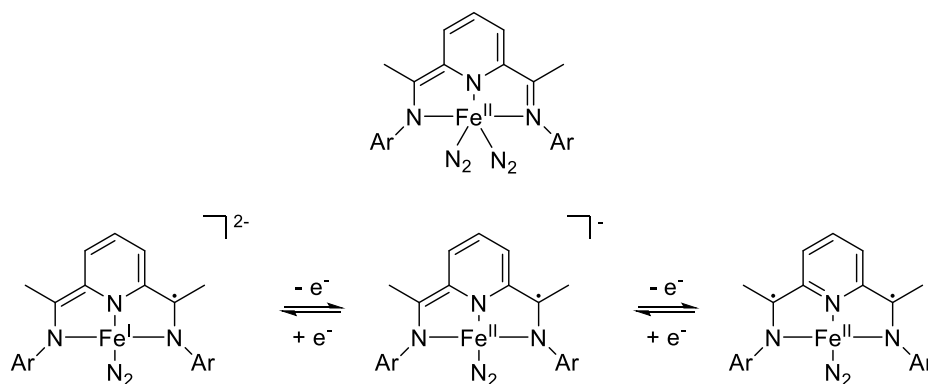
**Scheme 5:** Products of reactions between olefin and silane in the presence of catalyst.

In the past decade, there have been several hydrosilylation procedures that have been catalysed by Earth-abundant first row transition metals, such as iron. Chirik and co-workers reported one of the first examples of a well-defined iron complex for the anti-Markovnikov selective hydrosilylation of alkenes.<sup>27</sup> This method gave excellent yields for several substrates, including terminal alkenes such as styrene, internal alkenes such as cyclohexene and 1,1-disubstituted alkenes such as (+)-(*R*)-limonene (Scheme 6). The methodology was expanded to hydrogenation and hydroboration reactions, demonstrating the versatility of the complex.<sup>27,28</sup>

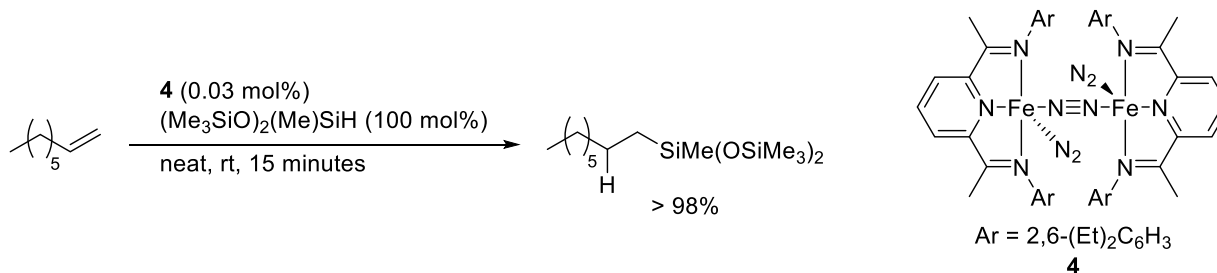


**Scheme 6:** Chirik's iron-catalysed hydrosilylation of alkenes.

The pre-catalyst used a bisiminopyridine ligand framework which is able to accept electron density (a redox non-innocent ligand), thus the complex could be viewed as a d<sup>6</sup> iron(II) complex in which the ligand has undergone a two-electron reduction (Scheme 7).<sup>29a</sup> Mossbauer spectroscopic studies further elaborated on the complex structure, revealing that it is best described as an intermediate spin iron(II) species with a diradical dianion ligand.<sup>29b</sup> Further studies demonstrated that one of the dimers of these complexes, **4**, was highly efficient for the selective *anti*-Markovnikov hydrosilylation of alkenes using sterically hindered tertiary silanes (Scheme 8).<sup>30</sup>



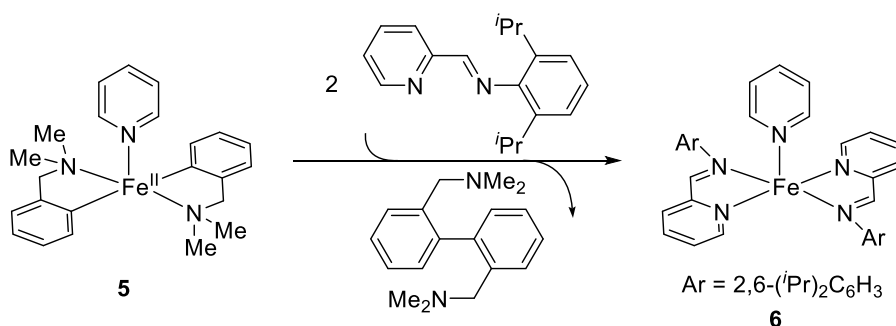
**Scheme 7:** Non-innocent character of the bisiminopyridine shown by Chirik and co-workers.



**Scheme 8:** Iron-catalysed hydrosilylation of alkenes with sterically hindered tertiary silanes.<sup>30</sup>

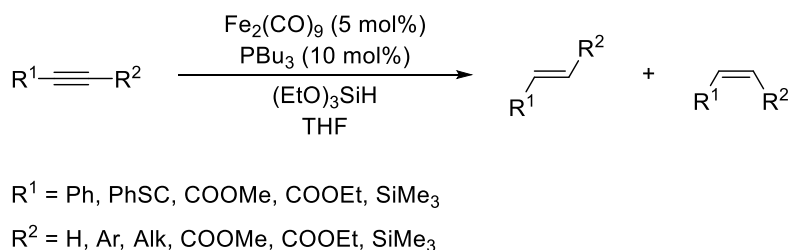
An alternative method of generating an active iron(0) complex was reported by Ritter and co-workers using a controlled reductive elimination of C-metallated benzylamine ligands (Scheme 9).<sup>31</sup> The ligands on the

pre-catalyst **5** are positioned such that the carbon donors are pseudo-*trans* to each other and thus unable to undergo a reductive elimination. Co-ordination of an iminopyridine ligand triggers ligand rearrangement into a *cis*-orientation, enabling reductive elimination to the formally iron(0) complex **6**. Due to the redox active nature of the iminopyridine ligands, however, the complex should be more correctly represented as iron(II). The oxidation state of the complex was confirmed using Mössbauer spectroscopy. This system was then applied to the regio- and stereoselective hydrosilylation of dienes. The pre-catalyst **5**, however, is not simple to prepare and cannot be stored for extended periods of time due to decomposition of the complex.



**Scheme 9:** Reductive elimination of ligand to generate an iron(0) complex.

The complexity in the syntheses of iron(0) complexes **3**, **4** and **6**, and the highly air- and moisture sensitive natures of these complexes, however, makes their use on a large scale impractical. There have been alternative methods reported using simpler systems, often in combination with a ligand that is either commercially available or easily synthesised, that can efficiently catalyse hydrosilylation. Complementary to Chirik's system, the formal reduction of alkynes to alkenes by a one-pot hydrosilylation and protodesilylation using mild conditions was developed by Enthaler.<sup>32</sup> Using a commercially available iron-carbonyl cluster with a simple phosphine ligand, high yields and very high stereoselectivity for the *cis*-alkene were observed (Scheme 10), although long reaction times (24 – 48 hours) were required in most cases and the reaction suffers from the inherent toxicity of the iron-carbonyl cluster.

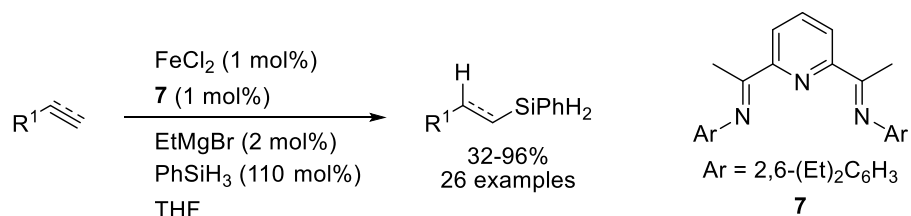


**Scheme 10:** Iron-catalysed formal reduction of alkynes by hydrosilylation and protodesilylation.

The use of iron(II) pre-catalysts for hydrosilylation has since been reported, generally using organometallic or hydride-containing reagents in order to generate an active catalyst *in situ*. The selective hydrosilylation

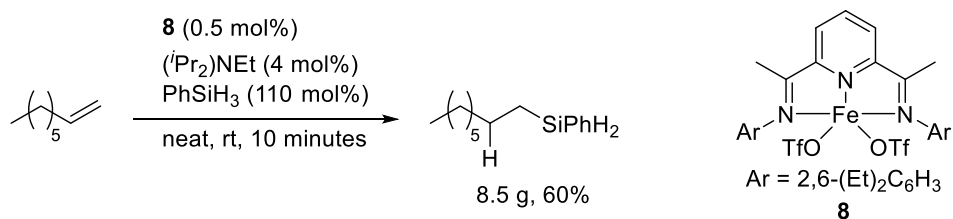


of terminal alkenes and alkynes using a commercially available source of iron salt with a bisiminopyridine ligand **7** was reported by Greenhalgh and Thomas.<sup>33</sup> This operationally simple methodology used a catalytic amount of Grignard reagent in order to form the active iron catalyst *in situ* (Scheme 11). Despite the presence of a Grignard reagent, high yields could be achieved even in the presence of functional groups such as carbonyls that are susceptible to nucleophilic attack.



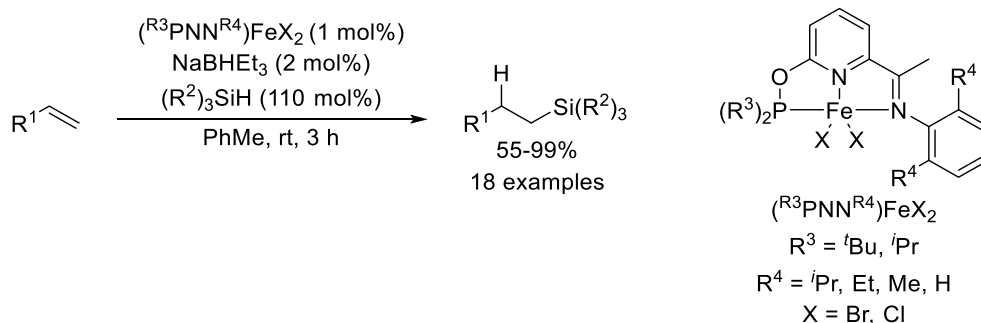
**Scheme 11:** Hydrosilylation of terminal alkenes and alkynes using an *in situ* activation method.

Further development of *in situ* activation methods led to the discovery of an iron-catalysed hydrosilylation using a bench-stable alkylamine to generate the active catalyst.<sup>34</sup> The method required the use of a bisiminopyridine iron triflate complex **8**, and *N,N*-diisopropylethylamine (Hunig's base) as the activator. Other amines were also used, although none proved as successful. The hydrosilylation of a number of alkyl alkenes and vinyl arenes was demonstrated, and functionalities including halides, carbonyls, imines and primary amines were all tolerated. A gram-scale hydrosilylation of 1-octene was carried out in the open air, which was a unique achievement in the field of iron-catalysed hydrofunctionalisation (Scheme 12).



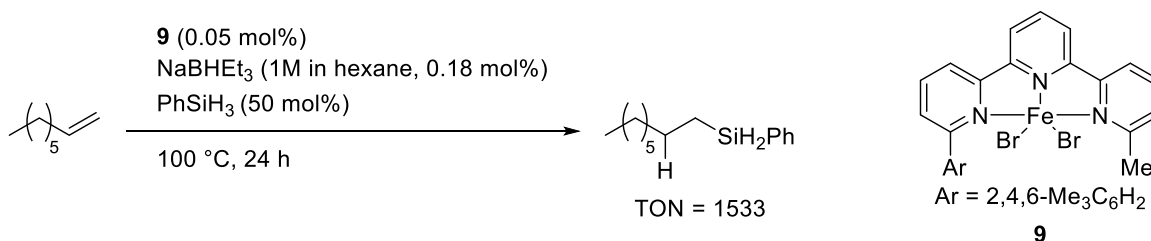
**Scheme 12:** Iron-catalysed gram-scale hydrosilylation carried out in the open air.

Ligands other than those based upon the bisiminopyridine framework have also been demonstrated to be effective for use in iron-catalysed hydrosilylation. Iron complexes using the structurally related phosphinite-iminopyridine ligand were shown to be highly chemoselective for the hydrosilylation of alkenes (Scheme 13).<sup>35</sup> This methodology used sodium triethylborohydride as an *in situ* activator. This presumably occurs through the formation of an iron dihydride species that can undergo reductive elimination to form an iron(0) complex. Under the reported conditions, alkene functionalisation took place in the presence of functionalities that are susceptible to reduction, including ketones, esters and amides. The reaction was, however, incompatible with several other functionalities including internal alkenes, free alcohols, allyl halides, secondary amides and alkenes conjugated to a pyridine ring.



**Scheme 13:** Hydrosilylation of terminal alkenes using an iron phosphinite-iminopyridine complex.

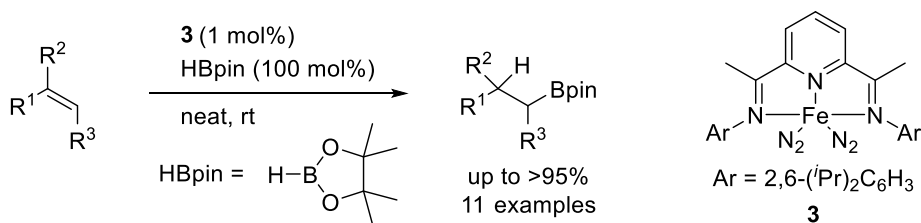
An iron complex with an unsymmetrically disubstituted terpyridine ligand, **9**, was reported to catalyse the hydrosilylation of alkyl alkenes by the group of Nakazawa (Scheme 14).<sup>36</sup> Similar to the above methodology, sodium triethylborohydride was used as the *in situ* activator. Interestingly, with this iron complex, changing the catalyst loading could change the selectivity of the reaction towards either a single or double hydrosilylation reaction which had not been reported previously. Despite the low catalyst loadings, these reactions did require high temperatures and long reaction times.



**Scheme 14:** Hydrosilylation of 1-octene using an iron terpyridine complex.

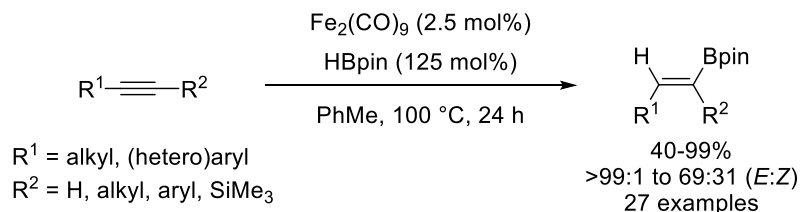
## 1.2.2: Hydroboration

The iron(0) dinitrogen complex **3** used for hydrosilylation was also found to be an effective catalyst for the *anti*-Markovnikov selective hydroboration of terminal, internal and 1,1-disubstituted alkenes, using pinacol borane (Scheme 15).<sup>28</sup> The hydroboration products were obtained in excellent yields with high regioselectivity for a variety of alkenes, although  $\alpha,\beta$ -unsaturated carbonyl compounds proved to be incompatible with the reaction. The reactions were run in neat alkene and pinacol borane, minimising waste from the use of solvent.

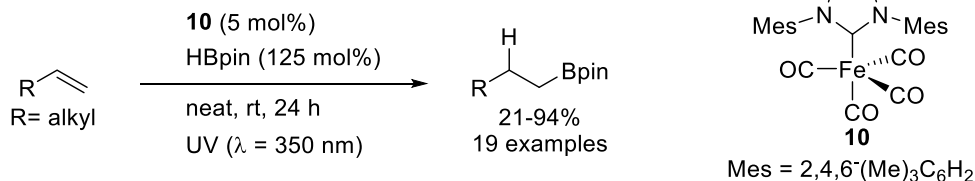


**Scheme 15:** Hydroboration of alkenes catalysed by an iron(0) dinitrogen complex.

Other iron(0) complexes such as those bound by carbonyl ligands were effective for the hydroboration of alkynes and alkenes. The carbonyl complex,  $\text{Fe}_2(\text{CO})_9$ , was demonstrated to be an effective pre-catalyst for the stereoselective hydroboration of terminal and internal alkynes, giving the (*Z*)-vinyl boronic ester as the major product in good to excellent yield (Scheme 16).<sup>37</sup> In this case, high temperatures were required to promote dissociation of a carbonyl ligand in order to activate the iron pre-catalyst for catalysis. By using the iron carbonyl pre-catalyst **10**, which contained an NHC ligand, the hydroboration of alkenes could be carried out at room temperature in the absence of solvent using continuous UV irradiation to activate the catalyst (Scheme 17).<sup>38</sup> The linear boronic ester product was obtained in all cases, even when an internal alkene was used which indicates alkene isomerisation can take place before the *anti*-Markovnikov addition of the pinacol borane. Several functionalities were tolerated under these conditions, including esters, acetals, epoxides and nitriles although yields were reduced in these cases.



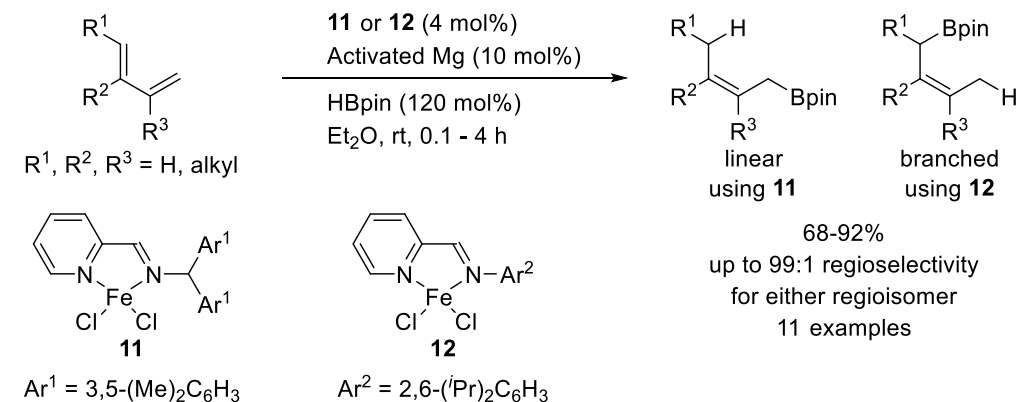
**Scheme 16:** Iron-catalysed hydroboration of alkynes using an iron carbonyl pre-catalyst.



**Scheme 17:** UV irradiation used to activate an NHC iron carbonyl complex for alkene hydroboration.

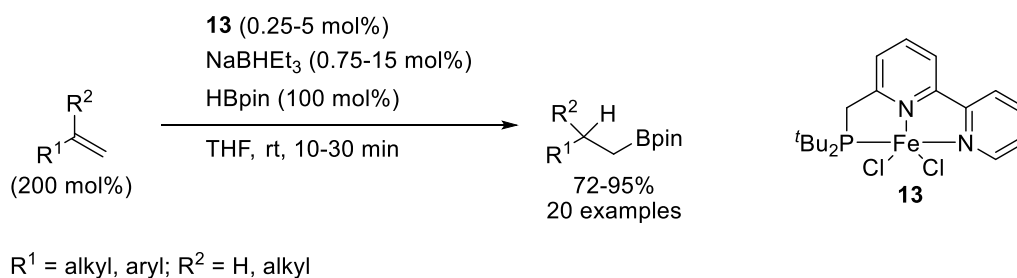
As with hydrosilylation, an *in situ* activation of the catalyst could be carried out eliminating the requirement for a low oxidation-state iron complex as the pre-catalyst. Allyl boronic esters could be formed by the 1,4-hydroboration of 1,3-dienes reported by Ritter, using the iminopyridine iron dichloride complexes, **11** and **12**, which were reduced *in situ* by activated magnesium (Scheme 18).<sup>39</sup> This methodology was regio- and stereoselective, with the (*E*)-isomer being isolated as the exclusive product. This reaction was particularly useful as the tri-substituted alkene products that were obtained in good yields can be otherwise synthetically

challenging to prepare. The selectivity was proposed to be due to the affinity for 1,3-dienes to low oxidation-state iron. The regioisomer obtained could be changed to either the linear or the branched product simply by changing the substitution on the imine nitrogen on the ligand.

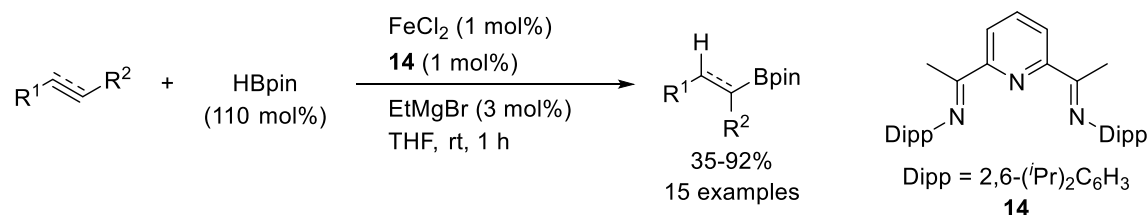


**Scheme 18:** Iron-catalysed 1,4-hydroboration of 1,3-dienes in high regio- and stereoselectivity.

Through the use of a tridentate phosphinobipyridine ligand, Huang demonstrated the hydroboration of unactivated terminal and 1,1-disubstituted alkenes, in good to excellent yields although an excess of the alkene was required (Scheme 19).<sup>40</sup> The high activity of the iron complex **13** was attributed to a high electron-density at the iron centre due to the donation of the three binding groups of the pincer ligand, and in particular the presence of phosphorus as a strong  $\sigma$ -donor, thus increasing electron density at the iron centre. Similarly, the tridentate bisiminopyridine ligand **14** could be used with iron(II) chloride to give a pre-catalyst that could be activated by a Grignard or organolithium reagent, which was then able to catalyse a hydroboration reaction with alkenes and alkynes (Scheme 20).<sup>41</sup> This reaction was more tolerant of functionalities than previous reactions, with free alcohols and amines and reducible groups such as esters and amides left untouched when submitted to the reaction conditions.

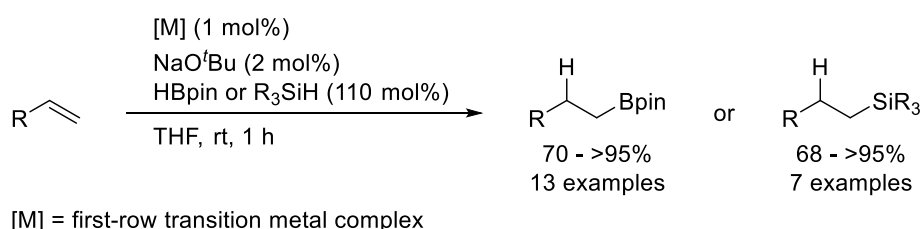


**Scheme 19:** Phosphinobipyridine iron(II) chloride complex as a pre-catalyst for terminal and 1,1-disubstituted alkene hydroboration.



**Scheme 20:** Alkene and alkyne hydroboration catalysed by an iron bisiminopyridine complex.

The *in-situ* activation of an iron pre-catalyst for the hydroboration and hydrosilylation of alkenes using an alkoxide salt has been reported recently by Thomas *et. al.* (Scheme 21).<sup>42</sup> This general method demonstrated that organometallic reagents were not required for pre-catalyst activation and repeated a range of literature reactions using the novel activation method, and showed new reactivity in other first-row transition metals such as cobalt, nickel and manganese. The proposed mechanism of activation proceeded through a hypervalent silicon-“ate” or boron-“ate” species to deliver a hydride to the metal centre. By using a sub-stoichiometric amount of either an organosilane or organoborane, it was shown that the method can be applied to reactions other than hydrofunctionalisation, such as  $[2\pi + 2\pi]$  alkene cycloaddition (Scheme 22).



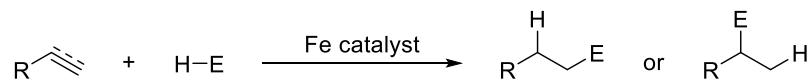
**Scheme 21:** The hydroboration and hydrosilylation of alkenes using an alkoxide salt as the pre-catalyst activator.



**Scheme 22:** An iron-catalysed  $[2\pi+2\pi]$  cycloaddition using an alkoxide salt as the pre-catalyst activator.

### 1.3: General Aims

The general aims of the research presented herein were to build upon the previous knowledge gained in iron catalysis and other metal-catalysed transformations and produce a novel methodology that could perform a variety of hydrofunctionalisations using a single set of reaction conditions (Scheme 23). This general method would ideally serve as a “one-pot” procedure and use commercially available starting materials, making it an easily accessible method for even the non-expert chemist.



- commercially available starting materials
- "one-pot" procedure
- single method, variety of products

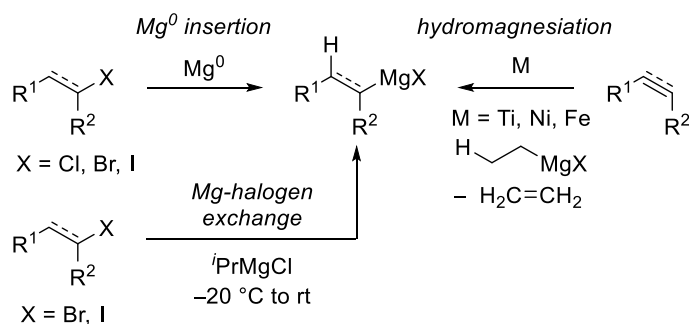
**Scheme 23:** General aims for the work described herein.

A secondary aim of discovering novel reactivity with Earth-abundant metals would also be targeted, and to possibly unlock new potential that thus far has yet to be exploited. Contained herein are three projects that followed this general aim. Firstly, in Chapter 2, the hydromagnesiation of alkenes and proceeding reactions with electrophiles all using a simple iron catalyst is described. With the potential of *in situ* Grignard reagent formation recognised, Chapter 3 describes some initial groundwork into the attempts on magnesium-catalysed hydroboration and hydrosilylation of alkenes and alkynes. Finally, using novel methodology discovered in the Thomas group, Chapter 4 describes a titanium-catalysed hydrosilylation of styrene derivatives using the commercially available titanocene dichloride.

## Chapter 2: Iron-Catalysed Hydromagnesiation of Vinylarenes and Dienes

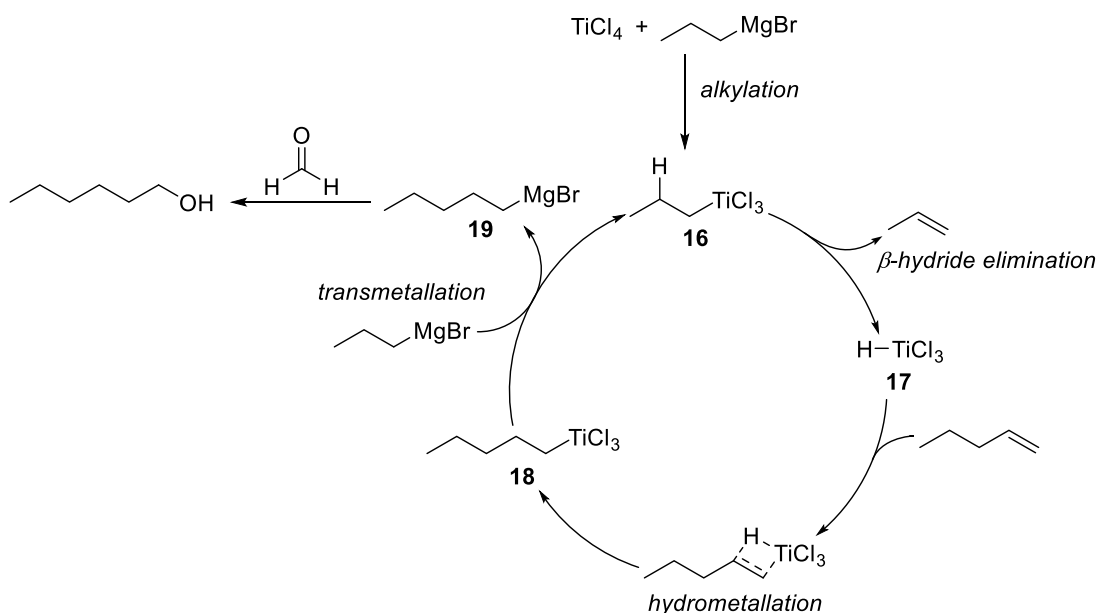
### 2.1: Introduction

Grignard reagents are highly versatile synthetic tools that can be used to construct a wide variety of bonds and introduce complexity into molecules.<sup>43</sup> The preparation of Grignard reagents typically involves the insertion of magnesium metal into a carbon-halogen bond (Scheme 24). However, the presence of sensitive functional groups and competitive Wurtz homocoupling can make the synthesis of some Grignard reagents challenging.<sup>44</sup> The formation of more functionalised organomagnesium reagents can be achieved using magnesium-halogen exchange.<sup>45</sup> As only the most electrophilic groups will react rapidly with Grignard reagents below 0 °C, with appropriate temperature control starting materials, containing esters, imines and other functionalities can be used.



**Scheme 24:** Preparation of Grignard reagents.

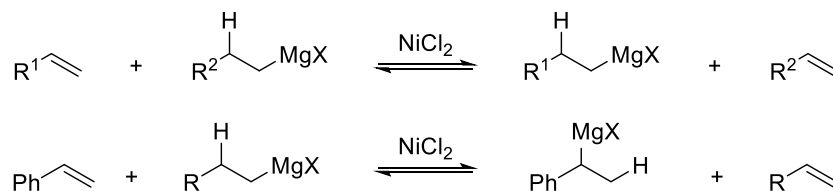
Alternatively, Grignard reagents can be prepared *via* hydromagnesiation, the formal addition of “H” and “Mg<sup>+</sup>” across alkenes and alkynes.<sup>46</sup> Hydromagnesiation was first reported by Cooper and Finkbeiner, who found that TiCl<sub>4</sub> was able to catalyse an exchange between alkylmagnesium halides and terminal olefins.<sup>47</sup> Upon addition of 1-pentene to *n*-propylmagnesium bromide in the presence of TiCl<sub>4</sub>, *n*-pentylmagnesium bromide was formed (Scheme 25). It was suggested that alkylation of the titanium pre-catalyst occurs at first to give the alkyltitanium compound **16**. Following this, β-hydride elimination can take place resulting in the formation of a titanium hydride species **17**. This species could then undergo hydrometallation to insert into the carbon-carbon double bond of 1-pentene, forming a second alkyltitanium compound **18** that is then able to undergo an exchange with magnesium to form the new Grignard reagent **19**.



**Scheme 25:** Cooper and Finkbeiner's titanium-catalysed hydromagnesiation.<sup>47</sup>

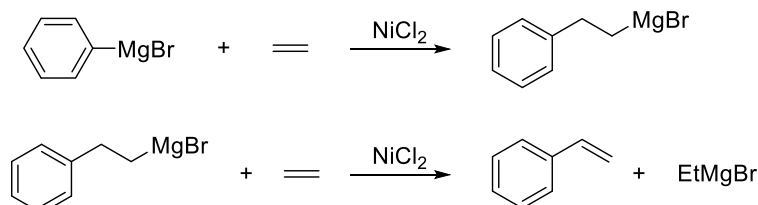
Subsequently, through continuation of the work by Cooper, Finkbeiner and others, it was found that other transition metals, such as nickel and iron, could act as catalysts for hydromagnesiation.<sup>48,49</sup>

Terminal alkenes were found to undergo an alkyl-olefin exchange with alkyl Grignard reagents catalysed by nickel chloride.<sup>48a</sup> The reaction was highly regioselective, giving the primary isomer as the major product, however, in the case of styrene, the secondary, benzylic product was obtained (Scheme 26). Internal alkenes, such as cyclohexene and 2-octene, were found to be inert under the reaction conditions. The nickel catalyst was also found to enable a carbomagnesiation reaction, wherein phenylmagnesium halides could insert across an alkene, in this case ethylene.<sup>48b</sup> A subsequent olefin-exchange reaction with a further equivalent of ethylene gave styrene as the product (Scheme 27). The nickel- and titanium-catalysed processes have been used in a number of organic syntheses, but generally require high temperatures and extended reaction times.<sup>50</sup>



**Scheme 26:** Nickel-catalysed hydromagnesiation of terminal alkenes and styrene.

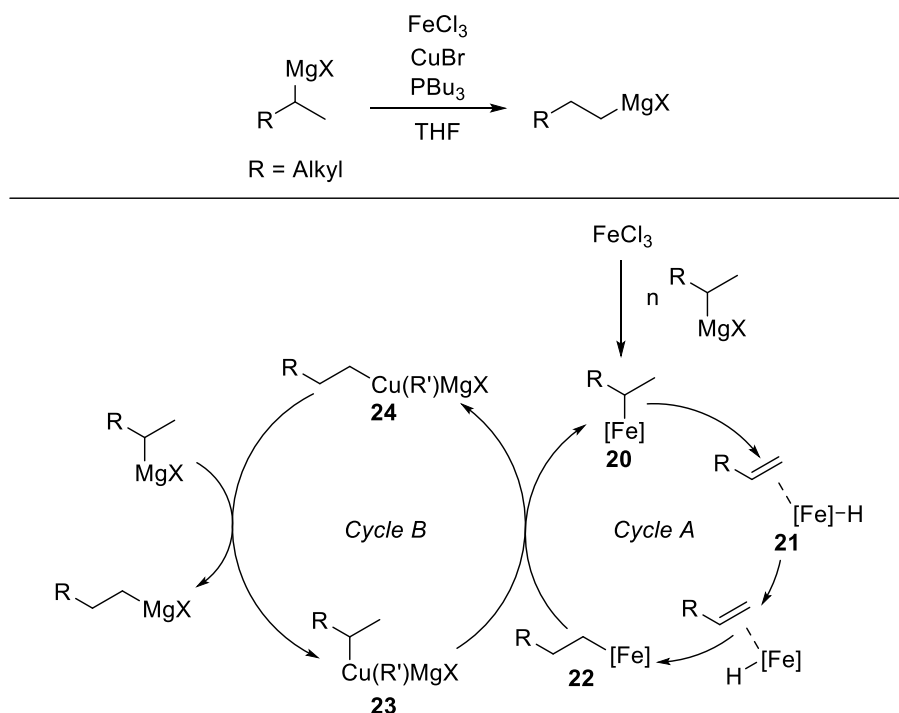




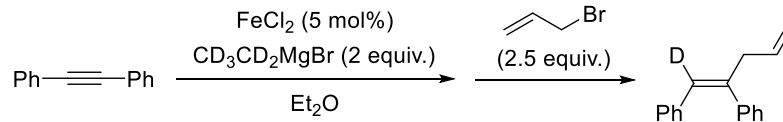
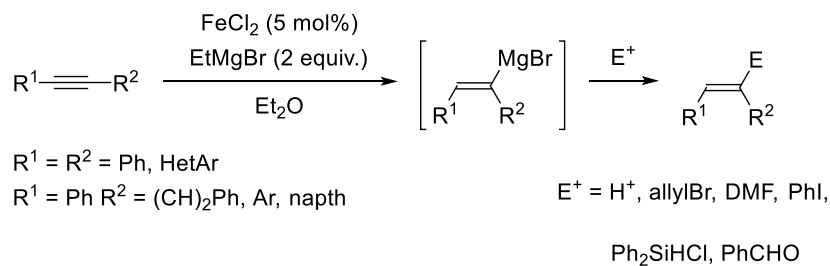
**Scheme 27:** Nickel-catalysed olefin insertion and subsequent exchange with ethylene.<sup>48b</sup>

Recently, several iron-catalysed hydromagnesiation reactions have been reported in high yields and under relatively mild conditions. Shirakawa and Hayashi reported the arylmagnesiation of alkynes, using iron and copper co-operative catalysis.<sup>51</sup> Using similar conditions, this system was subsequently applied to the isomerisation of secondary alkyl Grignard reagents to give thermodynamically favoured terminal alkyl Grignard reagents.<sup>52</sup> Their mechanistic studies suggested the iron catalyst was first alkylated by the Grignard reagent to give a secondary iron-alkyl species **20**. This was proceeded by a  $\beta$ -hydride elimination, giving an iron hydride species **21** as in Cooper and Finkbeiner's titanium mechanism (Scheme 28). The linear organoiron species **22** was then formed by a hydrometallation reaction (Cycle A).<sup>53</sup> The copper co-catalyst also reacts with the Grignard reagent, forming a cuprate species **23**. A transmetallation reaction can then take place between the organoiron **22** and cuprate species **23** to form the linear cuprate **24**. The reaction between this species and another equivalent of Grignard reagent gives the isomerised Grignard product (Cycle B). The isomerisation only occurred in very low yields ( $\leq 3\%$ ) in the absence of copper, indicating that the copper co-catalyst is required for the reaction to proceed catalytically. Under optimised conditions, a yield of 83% product with 99% regioselectivity was obtained.

Nakamura and co-workers reported the hydromagnesiation of diarylalkynes and diynes using a simple iron salt-catalysed system.<sup>54</sup> The reaction occurs quickly, under mild conditions and most notably can occur in the presence of functional groups that are known to be sensitive to reductive conditions. It is also worth noting that no competing carbomagnesiation took place under these conditions.<sup>51,55</sup> Linear primary alkyl Grignard reagents gave products in excellent yield, but the use of more sterically hindered or secondary Grignard reagents gave a much lower yield. By carrying out deuterium labelling experiments, it was shown that the hydride in this reaction was provided by the Grignard reagent (Scheme 29). Several alkyne substrates were also tested, obtaining good results with alkynes bearing both electron-withdrawing and electron-donating substituents. Increasing the steric demand of the alkyne had little effect on both reactivity and stereoselectivity. Alkynes bearing halogens also reacted in good yield, with little dehalogenation product being detected,<sup>56</sup> thus demonstrating a high affinity of the iron species for the alkyne.



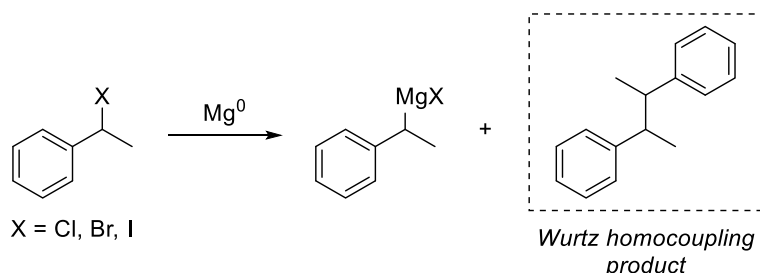
**Scheme 28:** Mechanism for Shirakawa and Hayashi's iron and copper-catalysed hydromagnesiation.<sup>52</sup>



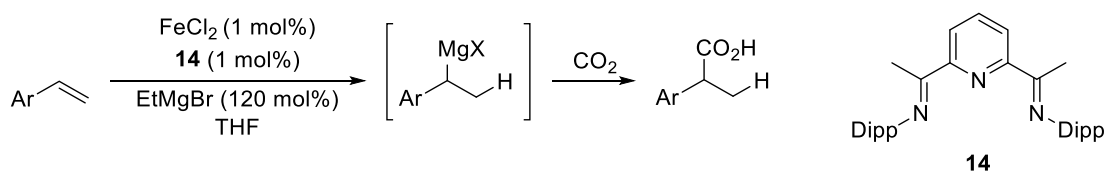
**Scheme 29:** Nakamura's hydromagnesiation of diaryl alkynes and deuterium studies.<sup>54</sup>

The formation of benzylic Grignard reagents by traditional methods is hindered by competing Wurtz homocoupling reactions (Scheme 30).<sup>44</sup> Thomas and co-workers reported the iron-catalysed hydrocarboxylation of styrenes, which proceeded by the hydromagnesiation of styrene derivatives to form a benzylic Grignard reagent (Scheme 31).<sup>57</sup> The reaction gave excellent yields with little to no homocoupled product detected, and with high regioselectivity, though the use of a bisiminopyridine ligand was required. This method of forming a Grignard reagent *in situ* was then used in the iron-catalysed synthesis of ibuprofen in an overall yield of 68% (Scheme 32).<sup>58</sup> In the same report, mechanistic studies were carried out with the aim of gaining a clearer understanding of the reaction in order to improve the catalytic system. It was found

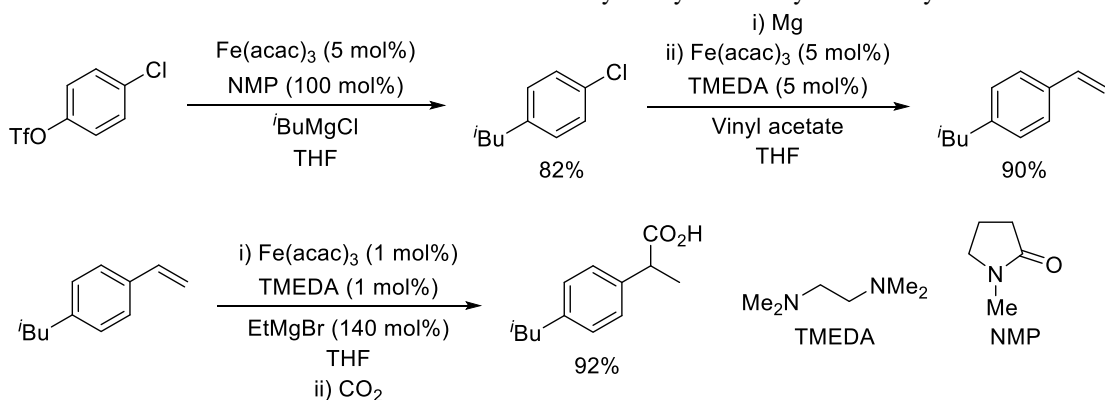
that the binding of ethene to the iron catalyst could inhibit the reaction and so the rate of loss of ethene from solution was an important factor to consider. To compensate for less efficient stirring in large-scale reactions, nitrogen was continuously bubbled through the reaction solution which resulted in the recovery of high catalytic activity.



**Scheme 30:** Formation of benzylic Grignard reagents by traditional methods.

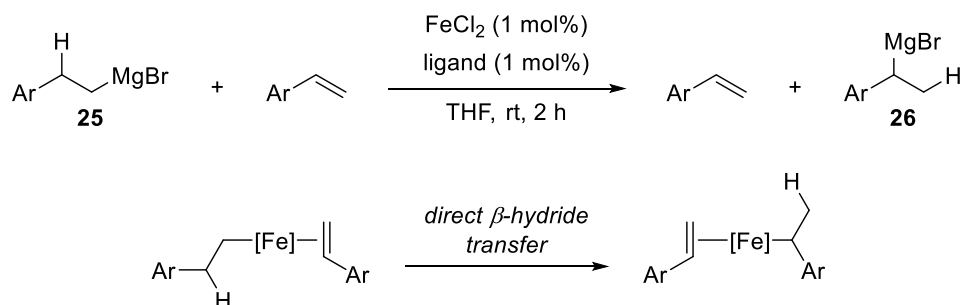


**Scheme 31:** Thomas and co-workers' iron-catalysed hydrocarboxylation of styrenes.<sup>57</sup>

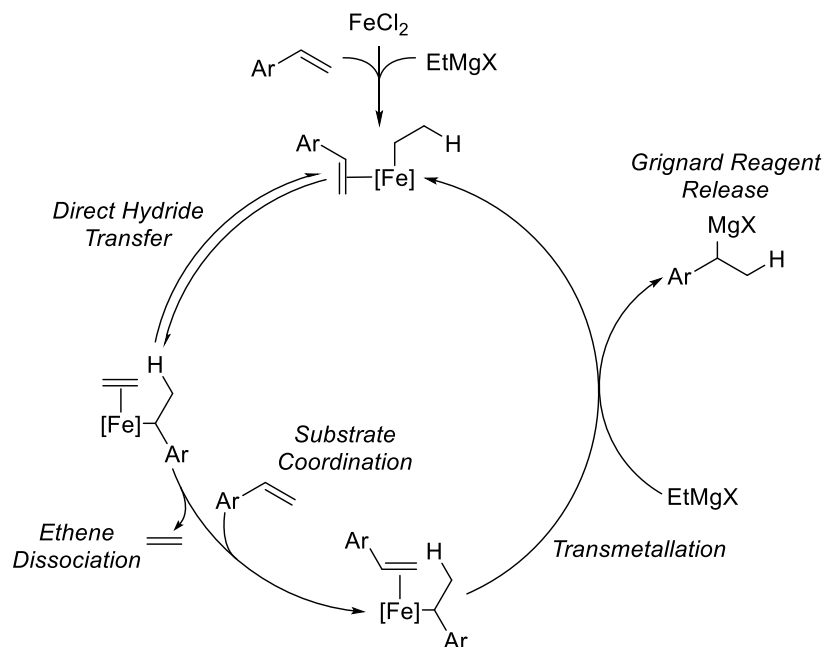


**Scheme 32:** Iron-catalysed three-step synthesis of Ibuprofen.<sup>58</sup>

Further in-depth mechanistic studies have revealed that the hydromagnesiation of styrene derivatives occurs through a  $\beta$ -hydride transfer mechanism, rather than the formation of an iron hydride species as proposed in previously published reports on hydromagnesiation.<sup>59</sup> This was discovered by submitting the homobenzylic Grignard reagent **25** to reaction conditions and then looking for isomerisation to the benzylic Grignard reagent **26** (Scheme 33). This isomerisation only occurs in the presence of an additional equivalent of alkene, which suggests that the mechanism does not proceed through a  $\beta$ -hydride elimination. A full catalytic cycle was proposed to proceed through a direct hydride transfer between an iron-alkyl and styrene to give a second iron-alkyl species, which then undergoes transmetallation to give the benzylic Grignard reagent (Scheme 34).



**Scheme 33:** Mechanism of hydride transfer in iron-catalysed hydromagnesiation.



**Scheme 34:** General mechanism for the iron-catalysed hydromagnesiation of styrene derivatives.

As isomerisation only occurred in the presence of an equivalent of a vinylarene, a direct hydride transfer mechanism as proposed in the nickel-catalysed hydromagnesiation of olefins is most likely taking place.<sup>48</sup> The hydride transfer mechanism is suggested to be facilitated by non-bonding orbitals of the metal, proceeding through a metal-hydride like transition state although the actual formation of a hydride complex is not necessary. In the absence of additional alkene, no isomerisation was observed and it could therefore be concluded that  $\beta$ -hydride elimination to give a metal-hydride complex does not take place in this reaction.

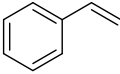
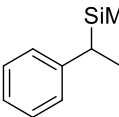
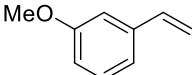
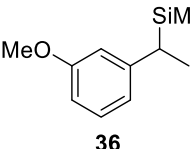
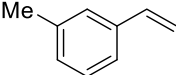
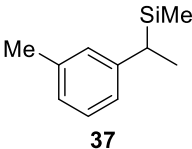
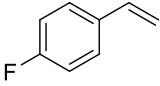
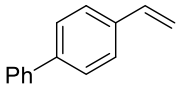
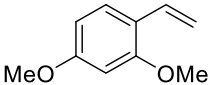
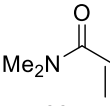
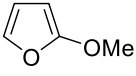
## 2.2: Results and Discussion

### 2.2.1: Hydromagnesiation of Vinylarenes

Previous work within the Thomas group had established a set of reaction conditions for the iron-catalysed hydrocarboxylation of styrene derivatives, and the substrate scope for this transformation had been explored.<sup>57,58</sup> Further optimisation found that the use of inexpensive iron salts and simple commercially available ligands such as 2,2'-bipyridine and *N,N,N',N'*-tetramethylenediamine were compatible with the reaction,<sup>60</sup> and the substrate scope was re-assessed to determine whether more electronically or sterically diverse substrates could be used with different electrophiles (Table 1). Substrates that were not commercially available could be synthesised in one step using the Wittig reaction (see Experimental section 5.2.2).

Under the new conditions, the formal hydrosilylation product **35** of styrene **27** was obtained in an excellent 90% yield (Table 1, Entry 1). Using the slightly electron-withdrawing 3-methoxy group led to similarly high yields, with the isolated product **36** obtained in a 73% yield (Table 1, Entry 2). Replacing the 3-methoxy group with a methyl group resulted in a reduction in the yield of hydrosilylation product **37** to 48% (Table 1, Entry 3). This reduction in yield may indicate an incompatibility of the reaction with electron-rich substrates, as the 3-methyl group is very slightly electron-donating ( $\sigma_m = -0.07$ ).<sup>61</sup> The reaction with 4-fluorostyrene **30** gave none of the products of hydromagnesiation (Table 1, Entry 4). It is possible that protodefluorination could take place as low oxidation-state iron may insert into the C-F bond.<sup>62</sup> This species would then be cleaved upon acidic work-up, giving styrene as the product. However, integration of the aromatic peaks in the <sup>1</sup>H NMR spectra gave a total of 4 protons, which suggests that 4-fluorostyrene starting material was still present. This does not rule out a very small amount of protodefluorination taking place, as the process may require stoichiometric levels of catalyst. This could be confirmed by carrying out a reaction with a 100 mol% loading of the iron-precatalyst and then determining whether the C-F remains intact over the course of the reaction. Both a biphenyl and disubstituted 2,4-dimethoxy species, **31** and **32**, were incompatible and resulted in polymerisation of starting material (Table 1, Entries 5 and 6). Two non-styrene derived alkenes were also screened, however in the case of *N,N*-dimethylacrylamide **33** no reaction took place, and 2-methoxyfuran **34** gave a complex mixture that was unable to be interpreted using <sup>1</sup>H NMR spectroscopy (Table 1, Entries 7 and 8).

**Table 1:** Screen of alkene substrate scope in iron-catalysed hydromagnesiation.

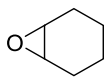
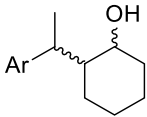

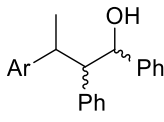
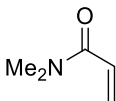
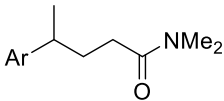
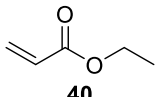
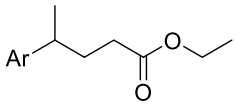
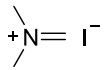
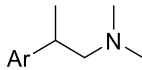
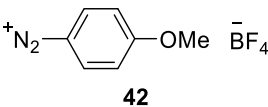
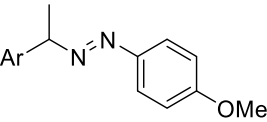
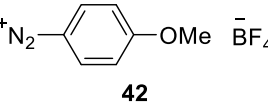
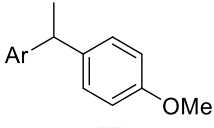
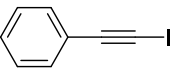
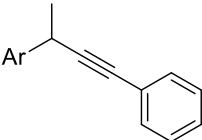
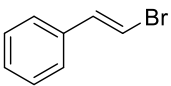
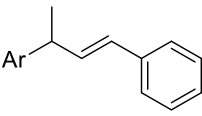
<div style="text-align: center;"> <math display="block">  \begin{array}{c}  \text{i) FeCl}_2 \cdot 4\text{H}_2\text{O (0.5 mol\%)} \\  \text{TMEDA (0.5 mol\%)} \\  \text{THF, rt, 2 h} \\  \text{ii) EtMgBr (3 M in Et}_2\text{O, 1.5 equiv.)} \\  \text{iii) Me}_3\text{SiCl (1.6 equiv.)}  \end{array}  \longrightarrow  </math> </div>			
Entry	Alkene	Product	Yield (%) <sup>a</sup>
1	 <b>27</b>	 <b>35</b>	90
2	 <b>28</b>	 <b>36</b>	73 <sup>b</sup>
3	 <b>29</b>	 <b>37</b>	48
4	 <b>30</b>	n/a	0 (96 S.M.)
5	 <b>31</b>	n/a	0 (polymerisation)
6	 <b>32</b>	n/a	0 (polymerisation)
7	 <b>33</b>	n/a	0
8	 <b>34</b>	n/a	Complex mixture by <sup>1</sup> H NMR

<sup>a</sup> Yield determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as internal standard.<sup>b</sup> Isolated yield.

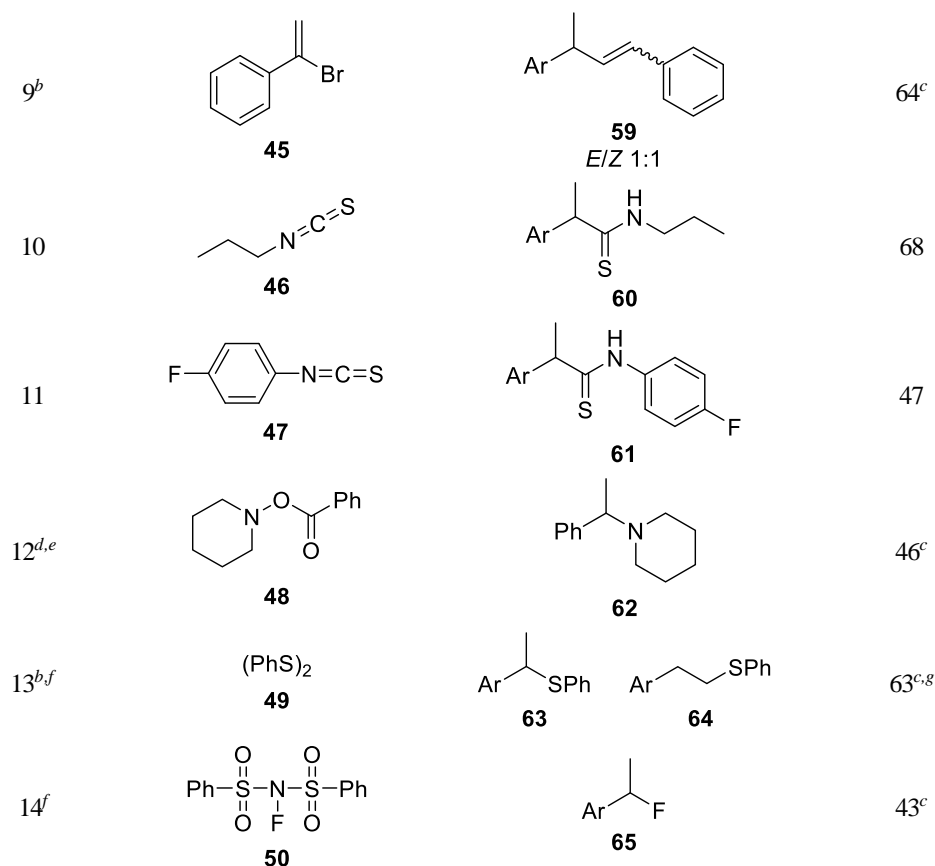
The electrophile scope was then explored in order to determine what functionality could be introduced using this reactivity. This work was conducted alongside Alison Jones and the most significant results were published in 2014.<sup>60</sup> The electrophile scope was conducted using 3-methoxystyrene **28** as a model substrate

(Table 2). A mono-substituted epoxide had already been shown to be successful and so disubstituted epoxides were investigated initially. The reaction with cyclohexene oxide **38** appeared to be successful, however product **51** has 3 stereocenters resulting in the formation of 8 diastereoisomers (Table 2, Entry 1). This mixture gave a complex  $^1\text{H}$  NMR spectrum that made it difficult to quantify a yield with this particular epoxide. The use of the more sterically hindered *trans*-stilbeneoxide **39** failed to give any alcohol product **52** (Table 2, Entry 2). The use of softer, alkene-based electrophiles was then attempted. Neither *N,N*-dimethylacrylamide **33** nor ethyl acrylate **40** reacted with the *in situ* generated Grignard reagent to give the functionalised products **53** or **54** (Table 2, Entries 3 and 4). Eschenmoser's salt **41** gave a very low yield of tertiary amine product **55** (Table 2, Entry 5). Using diazonium salt **42** resulted neither in product **56** from the reaction directly with the diazonium unit or the product from arylation, **57** (Table 2, Entries 6a and 6b). A formal hydroalkynylation was attempted using 1-iodo-2-phenylacetylene **43**, however the reaction gave a mixture of products that were inseparable by flash chromatography and could not be identified by spectroscopy (Table 2, Entry 7). Performing a hydrovinylation with  $\beta$ -bromostyrene **44** was, however, successful with alkene product **59** obtained in a 78% yield with complete stereoretention (Table 2, Entry 8). Interestingly, the reaction with  $\alpha$ -bromostyrene **45** gave the same product, **59**, in a 64% yield, albeit as a 1:1 mixture of stereoisomers (Table 2, Entry 9). Using alkyl and aryl isothiocyanates, **46** and **47**, resulted in high to moderate yields of the corresponding thioamide products, **60** and **61**, respectively (Table 2, Entries 10 and 11). A hydroamination was successfully carried out using *O*-benzoyl-*N*-hydroxypiperidine **48** as the nitrogen-containing electrophile, giving amine **62** in a moderate 46% yield (Table 2, Entry 12). Diphenyl disulphide **49** was an unusual electrophile as the regioselectivity was very different in this case, giving an inseparable 10:1 mixture of the  $\alpha$ - and  $\beta$ -regioisomers **63** and **64** in an overall 63% yield (Table 2, Entry 13). Hydrofluorination product **65** was formed in 43% yield after slightly modified reaction conditions were used (Table 2, Entry 14).

**Table 2:** Screen of electrophile scope in iron-catalysed hydromagnesiation

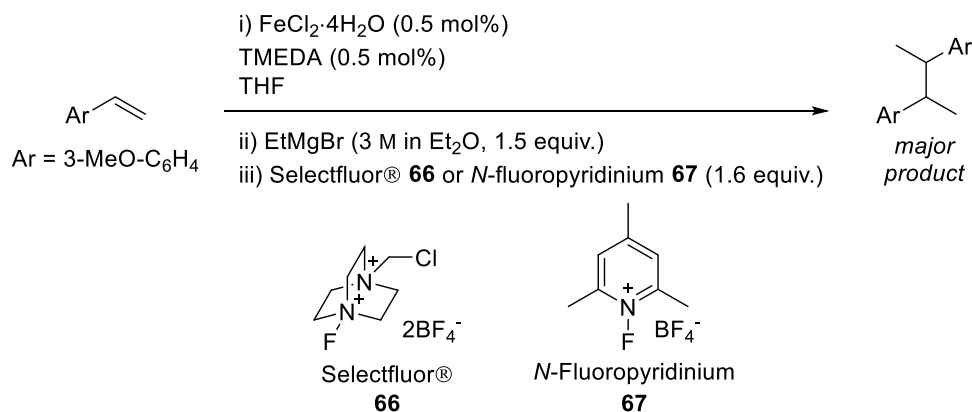
<div style="text-align: center;"> <math>\text{Ar}-\text{CH}=\text{CH}_2</math>  <math>\text{Ar} = 3\text{-MeO-C}_6\text{H}_4</math> </div> <div style="text-align: center;">           i) <math>\text{FeCl}_2 \cdot 4\text{H}_2\text{O}</math> (0.5 mol%)  <math>\text{TMEDA}</math> (0.5 mol%)  <math>\text{THF}</math>, rt, 2 h            ii) <math>\text{EtMgBr}</math> (3 M in <math>\text{Et}_2\text{O}</math>, 1.5 equiv.)            iii) <math>\text{E}^+</math> (1.6 equiv.)         </div> <div style="text-align: center;"> <math>\text{Ar}-\text{CH}(\text{Me})-\text{E}</math> </div>			
Entry	Electrophile ( $\text{E}^+$ )	Product	Yield (%) <sup>a</sup>
1	 <b>38</b>	 <b>51</b>	Complex mix of diastereoisomers
2	 <b>39</b>	 <b>52</b>	0
3	 <b>33</b>	 <b>53</b>	0
4	 <b>40</b>	 <b>54</b>	0 (polymerisation)
5	 <b>41</b>	 <b>55</b>	5
6a	 <b>42</b>	 <b>56</b>	0 (decomposition)
6b	 <b>42</b>	 <b>57</b>	0 (decomposition)
7	 <b>43</b>	 <b>58</b>	Mixture of products
8 <sup>b</sup>	 <b>44</b> <i>E/Z</i> 11:1	 <b>59</b> <i>E/Z</i> 13:1	78 <sup>c</sup>





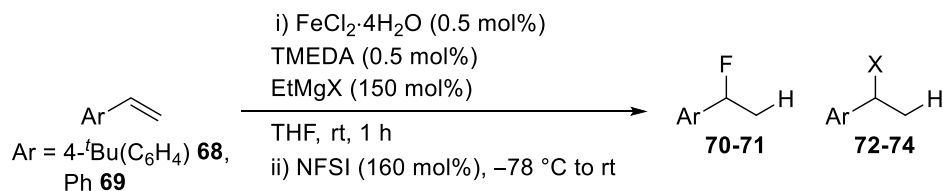
<sup>a</sup> Yield determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as internal standard. <sup>b</sup> Reaction carried out by Alison Jones. <sup>c</sup> Isolated yield. <sup>d</sup> Electrophile added at 0 °C as a solution in THF (1.0 M). <sup>e</sup> Styrene was used as substrate. <sup>f</sup> Electrophile added at -78 °C as a solution in THF (1.0 M). <sup>g</sup> Product isolated as a 10:1 mixture of  $\alpha$  and  $\beta$  regioisomers **63** and **64**.

A variety of different electrophilic fluorinating reagents were used in conjunction with the hydromagnesiation procedure. While it was found that Selectfluor® **66** and *N*-fluoropyridinium salt **67** failed to give any fluorination product, by lowering the temperature to -78 °C the reaction would proceed with *N*-fluorobenzenesulfonimide (NFSI) **50**. It was proposed NFSI was the only successful electrophilic fluorine source due to the oxidation potentials of the other reagents, with the homo-coupling product being observed in the <sup>1</sup>H NMR spectra when Selectfluor® **66** or *N*-fluoropyridinium salt **67** were used (Scheme 35). The redox potential of NFSI **50** is -0.78 V, compared to -0.73 V and -0.04 V for *N*-fluoropyridinium salt **67** and Selectfluor® **66**, respectively.<sup>63</sup> Previous studies have also shown that *N*-fluoropyridinium salts and NFSI are the most suitable electrophilic fluorinating reagents for use with Grignard reagents.<sup>64</sup>



**Scheme 35:** Hydromagnesiation reaction with other electrophilic fluorinating reagents.

Further investigation into the iron-catalysed formal hydrofluorination of styrene derivatives was carried out in an attempt to improve on the yields obtained. In a number of the reactions performed, a significant amount of the  $\alpha$ -bromo side-product was observed and so different Grignard reagents were screened in an attempt to suppress this (Table 3). The reaction with ethylmagnesium chloride gave only the 1-chloroethyl benzene product **72** in 40% yield with no hydrofluorination product **70** observed. Using the standard conditions, only a 20% yield of the hydrofluorination product **70** was observed in comparison to a 43% yield with 4-methoxystyrene **28** (Table 2, Entry 14). This is most likely down to electronic effects on the aromatic ring. The 1-bromoethyl product **73** was observed in a 14% yield. Ethylmagnesium iodide was independently synthesised and used in a reaction. This gave the product, (1-fluoroethyl)benzene **71**, albeit only in 22% yield. (1-Iodoethyl)benzene **74** was also observed in very small yield (3%). It was thought that **74** could have undergone homocoupling under reaction conditions, however on analysis by  $^1\text{H}$  NMR spectroscopy there was only a slight increase in the amount of homocoupling product compared to that which was usually observed. From these results, there is a trend of decreasing yield of unwanted halogenated side-product as one moves down group 17. It then seems that this halogenation could occur *via* one of two possible mechanisms. One pathway would be the radical abstraction of the halogen, as it is known that chlorine is more susceptible to radical abstraction than bromine or iodine.<sup>43</sup> Another possible mechanism would be the oxidation of  $\text{MgCl}_2$  salt to form  $\text{Cl}^+$  ions which would then be susceptible to nucleophilic attack by the Grignard reagent.

**Table 3:** Iron-catalysed formal hydrofluorination using different halides in the Grignard reagent.

Entry	EtMgX	70-71 (%) <sup>a</sup>	72-74 (%) <sup>a</sup>
1	EtMgCl	0	40
2	EtMgBr	20	14
3 <sup>b</sup>	EtMgI	22	3

<sup>a</sup> Yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as an internal standard. <sup>b</sup> Styrene was used.

In order to determine whether the iron catalyst plays a role in the interaction between electrophiles and *in situ* generated benzylic Grignard reagent, an independently synthesised benzylic Grignard reagent **75** was prepared and reacted with a selection of electrophiles (Table 4). In the absence of an iron catalyst, NFSI **50** was the only electrophilic fluorinating reagent to react with the benzylic Grignard reagent **75**, reflecting what was seen in the iron-catalysed hydromagnesiation procedure (Table 4, Entries 1 – 3). As with the iron-catalysed procedure, the homo-coupling product was observed, although this may be present in the reaction mixture leftover from the formation of the benzylic Grignard reagent **75**. An attempt to use electrophilic trifluoromethylating reagent **76** was unsuccessful (Table 4, Entry 4). The reaction with diphenyl disulphide **49** gave a similar yield to the hydromagnesiation procedure, although there was none of the linear product present which results from the isomerisation of the benzylic Grignard reagent in the presence of iron (Table 4, Entry 5).  $\beta$ -Bromostyrene **44** also gave a comparable yield to the hydromagnesiation reaction, however when  $\alpha$ -bromostyrene **45** was used, the same product was observed albeit in a lower yield (Table 4, Entries 6 and 7). This result indicates that the presence of iron may be necessary for this reaction and that the vinylic bromide electrophiles may react through an addition-elimination type mechanism rather than any cross-coupling like mechanism (Scheme 36). Due to the stereospecificity of the reaction with  $\beta$ -bromostyrene **44**, the mechanism is unlikely to proceed *via* an alkenyl radical that would be prone to racemisation.<sup>65</sup> This does not, however, entirely rule out a single-electron transfer mechanism as has been reported previously for the metal-free cross-coupling of aryl Grignard reagents with alkenyl halides.<sup>66</sup>

These results demonstrate that the Grignard reagent largely acts independently, and the iron catalyst is only required for the hydromagnesiation reaction. As the benzylic Grignard reagent is the thermodynamically most stable product, the regiochemistry is set at this position and, with a few exceptions, the branched

product is formed exclusively. Any other regio- or stereochemical outcome is determined by the interaction between the Grignard reagent and electrophile only.

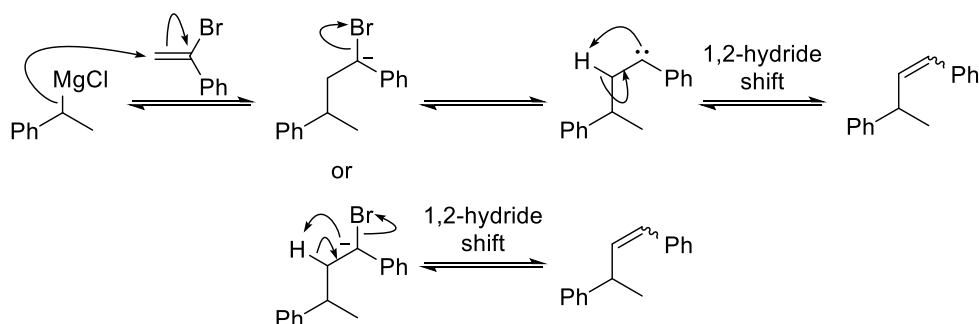
**Table 4:** Reactions of electrophiles with independently synthesised Grignard reagent.

$\text{Ph}-\text{CH}(\text{CH}_3)-\text{MgCl} \xrightarrow[\text{THF}]{\text{Electrophile (1.6 equiv.)}} \text{Ph}-\text{CH}(\text{CH}_3)-\text{E}$

**75**

Entry	Electrophile	Yield (%) <sup>a</sup>	Yield under standard conditions (%)
1	<p><b>50</b></p>	55	43
2	<p><b>66</b></p>	0	0
3	<p><b>67</b></p>	0	0
4	<p><b>76</b></p>	0	n/a
5	<p><b>49</b></p>	56	63 <sup>b</sup>
6	<p><b>44</b></p>	65	78 <sup>c</sup>
7	<p><b>45</b></p>	<10 <sup>d</sup>	64 <sup>d</sup>

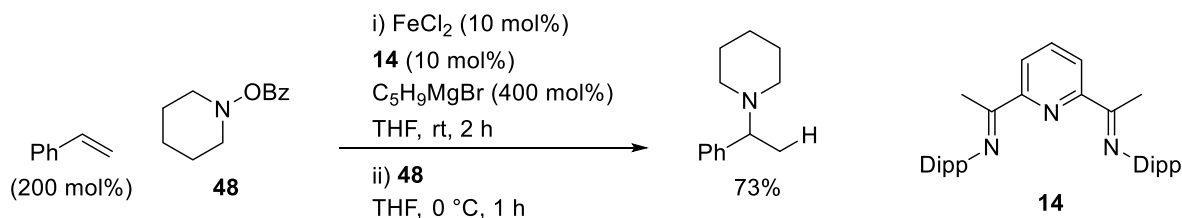
<sup>a</sup> Yield determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as internal standard. <sup>b</sup> Product isolated as a mixture of  $\alpha$  and  $\beta$  regioisomers. <sup>c</sup> *E/Z* stereoisomers in a 13:1 ratio. <sup>d</sup> *E/Z* stereoisomers in a 1:1 ratio.



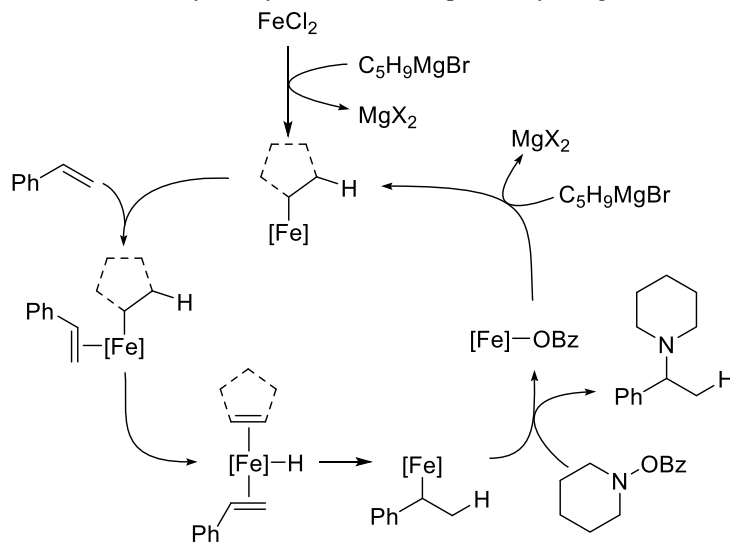
**Scheme 36:** Potential addition-elimination mechanism for  $\alpha$ -bromostyrene.

## 2.2.2: Study on the Reactive Organometallic Species

Shortly before the publication of this hydromagnesiation work, an iron-catalysed hydroamination of styrene derivatives was published by Yang and co-workers using similar reaction conditions (Scheme 37).<sup>67</sup> Despite the similarity of the conditions to the hydromagnesiation method, it was proposed that a low oxidation-state iron alkyl species reacted directly with the electrophile in order to turn over the catalytic cycle (Scheme 38).



**Scheme 37:** Iron-catalysed hydroamination reported by Yang and co-workers.



**Scheme 38:** Mechanism proposed by Yang for the hydroamination of styrene derivatives.

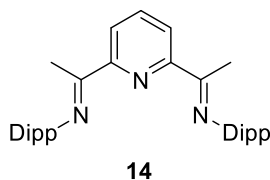
Thus, a need to clarify the active nucleophilic organometallic intermediate was apparent. The validity of a

reaction between a benzylic Grignard reagent and the electrophilic amine reagent was first examined, by reacting an independently synthesised Grignard reagent **77** with the electrophilic amination reagent **48** under different sets of conditions (Table 5). In the absence of any iron and with both Grignard reagents, **77** and **78**, present, the hydroamination product **61** was observed in high yields (Table 5, Entries 1 and 2). When iron pre-catalyst from both the hydromagnesiation and hydroamination reactions were included the yield of **61** was largely unchanged, indicating the presence of iron had no impact upon the reaction between Grignard reagent and electrophile (Table 5, Entries 3 and 4). Upon establishing a background reaction between a benzylic Grignard reagent and *O*-benzoyl-*N*-hydroxypiperidine under both sets of conditions, it was necessary to determine whether both reactions proceeded through a single mechanism.

**Table 5:** Examining the reactivity between benzylic Grignard reagent and *O*-benzoyl-*N*-hydroxypiperidine.

Entry	<b>77</b> (mol%)	<b>78</b> (mol%)	[Fe] (mol%)	ligand (mol%)	<b>61</b> (%) <sup>a</sup>
1	100	-	-	-	61
2	200	200	-	-	70
3	100	-	FeCl <sub>2</sub> ·4H <sub>2</sub> O (0.5)	TMEDA (0.5)	69
4	200	200	FeCl <sub>2</sub> (10)	<b>14</b> (10)	63

<sup>a</sup> Yield determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as internal standard.



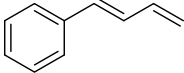
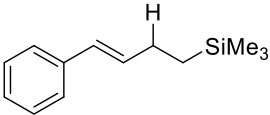
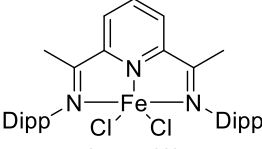
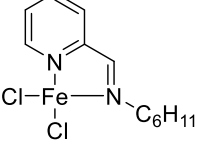
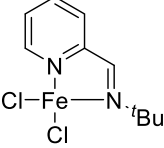
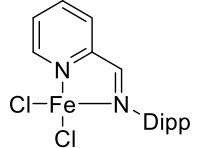
Under the mechanism proposed by Yang, the catalytic cycle was turned over by the reaction with an electrophile whereas under the Thomas group mechanism, a stoichiometric amount of a reactive organometallic is formed and then reacted with the electrophile. Therefore, by removing the electrophile from the system, the mechanism can be clarified. Reactions under both the hydromagnesiation reaction conditions reported above and Yang's hydroamination reaction conditions, in the absence of an electrophile, were monitored by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy (see Experimental, Section 6.2.8, p. 86). In both cases, >95% of the starting material had been converted to an organometallic species as observed by <sup>1</sup>H NMR

spectroscopy. As stoichiometric conversion of starting material had taken place, the organoiron species cannot be participating as the active nucleophilic species as catalytic turnover could not take place without the electrophile. Yang's hydroamination reaction used a 10 mol% loading of iron pre-catalyst and so following the hydroamination mechanism, only 10% of starting material should have been converted to a reactive intermediate. By comparing the observed peaks in the  $^1\text{H}$  and  $^{13}\text{C}$  spectra to those previously reported in a hydromagnesiation study,<sup>58</sup> it could be determined that the reactive organometallic intermediate being formed in both cases was the benzylic Grignard reagent **77**.

### 2.2.3: Hydromagnesiation of Dienes

As the scope of the hydromagnesiation reaction was limited to styrene derivatives, an investigation into a broader alkene scope was carried out. Phenyl dienes were identified as a potential target as a simple extension of the conjugated system may still be compatible under similar reaction conditions. An initial screen for catalysts was conducted using phenyl-1,3-butadiene **79** as a model substrate reacting with trimethylsilyl chloride to give a formal 1,2-hydrosilylation product **80** (Table 6). Using the same iron salt and ligand as the styrene hydromagnesiation, but at a slightly higher loading, gave 1,2-hydrosilylation product **80** in a 40% yield (Table 6, Entry 1). Similar results were obtained when using an iron(III) pre-catalyst (Table 6, Entry 2), however using the bisiminopyridine complex that had proved successful for other reactions gave none of the formal hydrosilylation product (Table 6, Entry 3). By switching from a tridentate ligand to a bidentate iminopyridine ligand, moderate yields were again achieved (Table 6, Entries 4 and 5), however when large substituents on the imine were used, the reactivity was lost once again (Table 6, Entry 6).

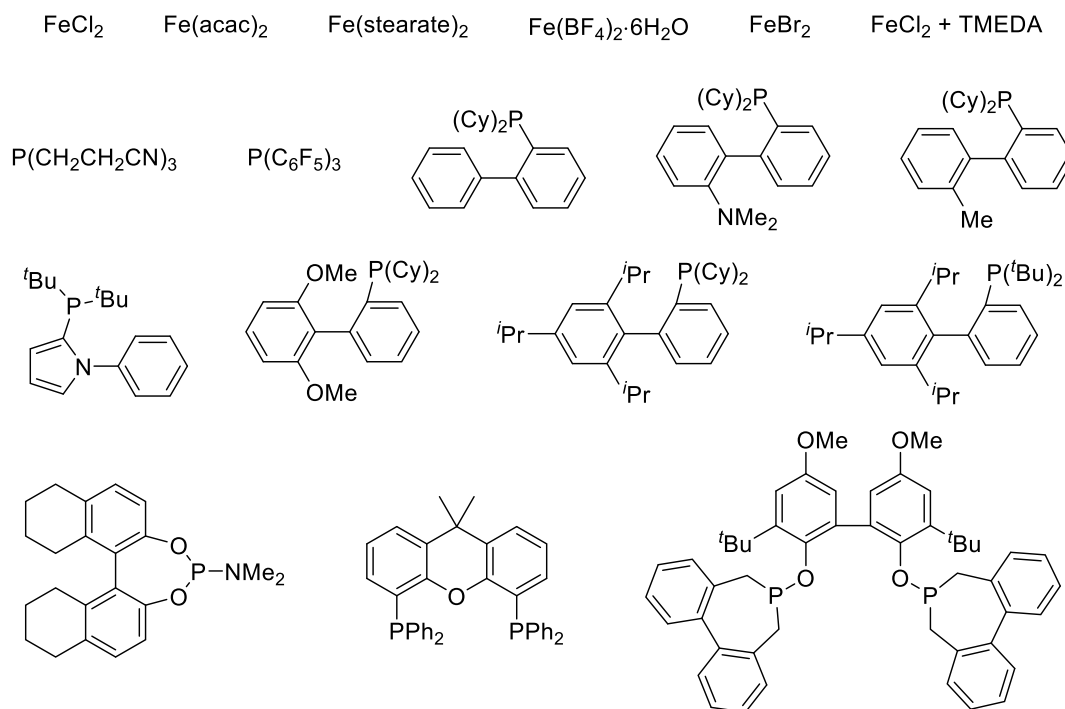
**Table 6:** Initial catalyst screen for the hydromagnesiation of 1,3-dienes.

<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;">  <p><b>79</b></p> </div> <div style="text-align: center;"> <p>i) [Fe] (5 mol%) Ligand (10 - 20 mol%)</p> <hr style="width: 50%; margin: 0 auto;"/> <p>EtMgBr (3 M in Et<sub>2</sub>O, 150 mol%) THF, rt, 30 min to 2 h ii) Me<sub>3</sub>SiCl (160 mol%) rt, 2 h</p> </div> <div style="text-align: center;">  <p><b>80</b></p> </div> </div>		
Entry	[Fe]/Ligand	Yield (%) <sup>a</sup>
1	FeCl <sub>2</sub> ·4H <sub>2</sub> O (5 mol%) TMEDA (5 mol%)	40
2	Fe(acac) <sub>3</sub> (5 mol%) TMEDA (5 mol%)	35
3	 (5 mol%)	-
4	 (5 mol%)	34
5	 (5 mol%)	25
6	 (5 mol%)	-

<sup>a</sup> Yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as an internal standard.

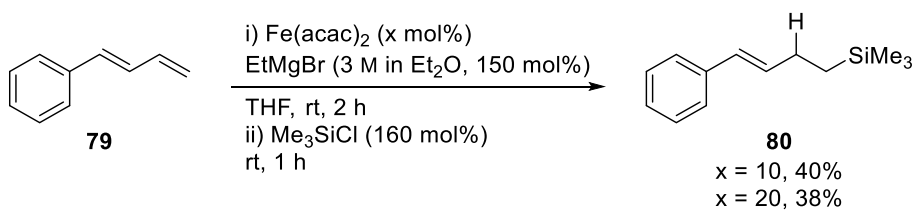
As no significant improvements in the yield were found in the initial screen, a more in-depth investigation was carried out using a range of different iron salts and phosphine ligands, traditionally used in cross-coupling reactions (Scheme 39; see Experimental, Section 6.3.3, p. 94 for further details). Unfortunately, none of these combinations resulted in any satisfactory increase in the yield of product **80** and so further experiments were carried out using the Fe(acac)<sub>2</sub> salt.



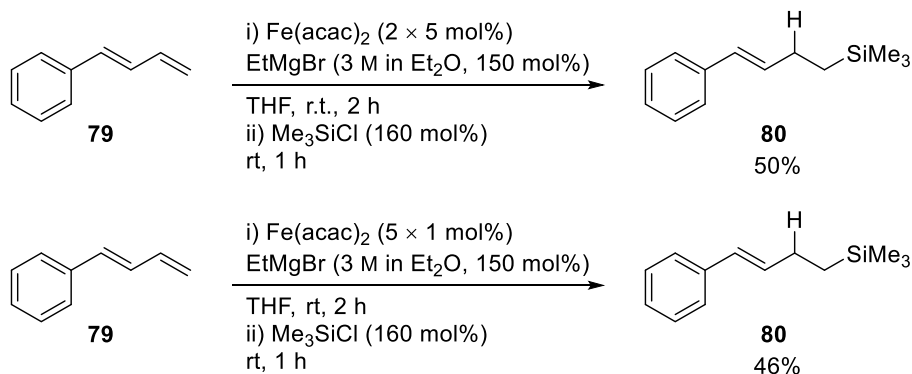


**Scheme 39:** Iron salts and ligands used for catalyst screen of 1,3-diene hydromagnesiation.

An increase in the catalyst loading from 5 mol% to 10 and 20 mol% gave product **80** in the same yield as that previously observed (40% and 38%, respectively) (Scheme 40). The addition of a second portion of catalyst after 30-minutes gave a slightly improved yield of 50%, however adding smaller portions at 20-minute time intervals gave no further improvement in yield (46%) (Scheme 41). Using a large excess of Grignard reagent and electrophile only resulted in a reduction of product yield.



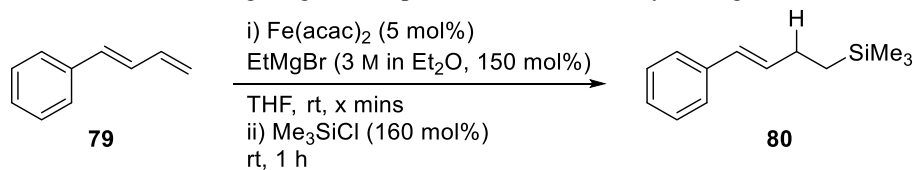
**Scheme 40:** Increased catalyst loading for 1,3-diene hydromagnesiation.



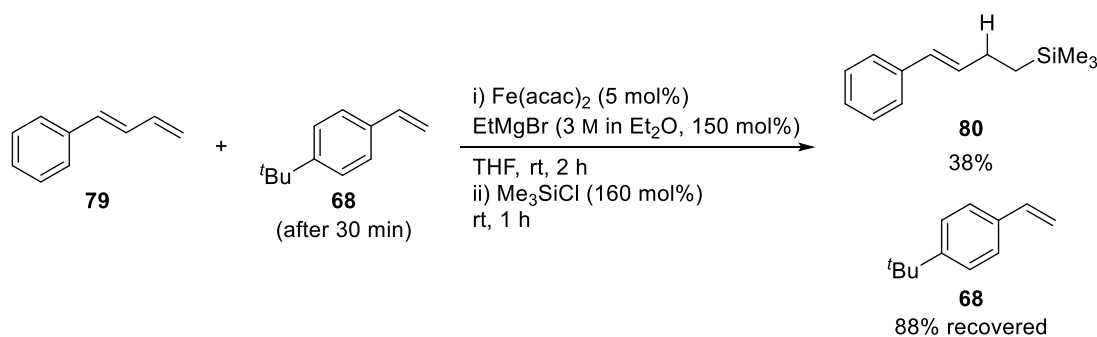
**Scheme 41:** Addition of catalyst portion-wise.

As changes to the catalyst system were having little effect on the product yield, the time required for the reaction to reach completion was investigated. Firstly, a reaction was carried out with only a 30-minute stirring time for the hydromagnesiation. After quenching, 1,2-hydrosilylation product **80** was obtained in a 36% yield, indicating the reaction was reaching completion faster than with styrene derivatives. Following this result, a series of aliquots were taken from an iron-catalysed 1,3-diene hydromagnesiation reaction to determine where the reaction end point was (Table 7). From this data, it was seen that quenching the reaction after just 30 seconds resulted in a 42% yield of 1,2-hydrosilylation product **80**, indicating that the reaction was taking place extremely quickly. It could be possible, however, that after this short time period that no further reaction with 1,3-diene **79** takes place but the catalyst is still active. In order to test this, a competition reaction was set up where an equivalent of 4-*tert*-butylstyrene **68** was added to the hydromagnesiation reaction after a 30-minute time period. As expected, the hydrosilylation product of the 1,3-diene, **79**, was found in a 36% yield, however, most of the 4-*tert*-butylstyrene **68** was recovered (Scheme 42). This indicates that the catalyst was becoming inactive after a short period of reaction. One possible explanation for this would be that some portion of the starting material is polymerising and trapping the active iron species within the polymer, preventing any further reaction. It is also possible that unlike the system with styrene derivatives, the two binding sites of the 1,3-diene result in a co-ordinatively saturated metal centre that is unable to take part in further reactivity.

**Table 7:** Investigating the end point of the 1,3-diene hydromagnesiation.



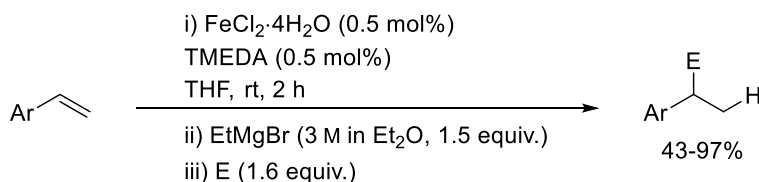
Time (min)	Yield (%)	Time (min)	Yield (%)
0.5	42	10	36
1	41	30	40
1.5	42	60	36
2	38	90	40
5	44	120	35



**Scheme 42:** Competition reaction between 1-phenyl-1,3-butadiene and 4-*tert*-butylstyrene.

## 2.3: Conclusions and Future Work

The hydromagnesiation of styrene derivatives was found to be an excellent methodology for the introduction of new functionality. Although the substrate scope was limited to styrene derivatives, a wide range of electrophiles were compatible with the system for the generation of new carbon-carbon and carbon-heteroatom bonds, including the products of a formal hydrofluorination using a source of electrophilic fluorine (Scheme 43).



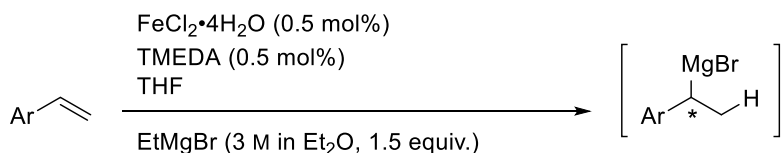
E = C(sp<sup>3</sup>), C(sp<sup>2</sup>), RC=O, RC-N/O, B(OR)<sub>2</sub>, NR<sub>2</sub>, OH, SiMe<sub>3</sub>, F

**Scheme 43:** General scheme for iron-catalysed hydromagnesiation of styrene derivatives.

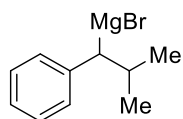
The reactions proceeded with extremely high regioselectivity, determined by the highly stable, conjugated benzylic anion. The key intermediate was shown, in all cases, to be the benzylic Grignard reagent formed *in situ* which then reacts with the chosen electrophile. The iron catalyst was only required for the hydromagnesiation reaction itself. Extension of the reaction to a more conjugated 1,3-diene had limited success, with only 40% yield of the 1,2-hydrosilylation product being observed. Further investigation showed that the catalyst was only active for a very short amount of time in these cases.

The system would be greatly improved if the substrate scope could be expanded to include internal alkenes, for example  $\beta$ -methylstyrene could be used as a model substrate. This would allow for the methodology to be used towards several pharmaceutically relevant targets. Despite internal alkynes being shown to be compatible in previous hydromagnesiation reactions,<sup>54</sup> the hydromagnesiation of internal alkenes is so far unknown.

The hydromagnesiation of styrene derivatives could easily be imagined to be developed further towards an enantioselective variant, based on the products generated (Scheme 44). This would entirely depend on the rate of racemisation of the benzylic Grignard reagent generated, as if sufficiently fast then a racemic mixture would be expected. The racemisation of a benzylic Grignard reagent **81** was shown to be  $<0.02\text{ s}^{-1}$  by Brown and co-workers (Figure 1),<sup>68</sup> although initial investigations into the *in situ* generated benzylic Grignard reagents within the Thomas group have been inconclusive as to whether this rate of racemisation is slow enough to allow for an enantioselective reaction.<sup>69</sup>



**Scheme 44:** Stereocenter generated through the hydromagnesiation of styrene derivatives.



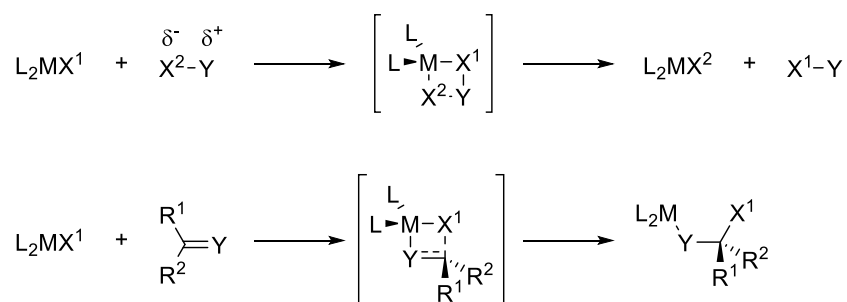
**81**

**Figure 1:** Benzylic Grignard reagent used in studies by Brown and co-workers.<sup>62</sup>

## Chapter 3: Magnesium-Catalysed Hydrosilylation and Hydroboration

### 3.1: Introduction

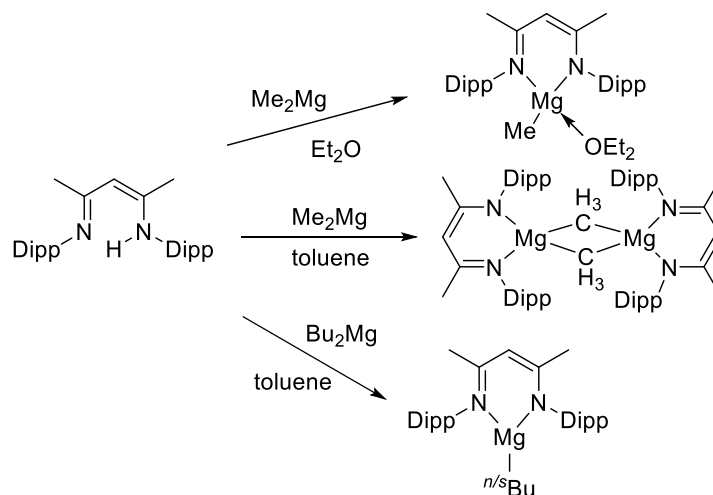
Despite the abundance of the alkaline-earth metals, such as magnesium and calcium, their potential as catalysts remains under-developed. Due to the high energy d orbitals of the alkaline-earth metals, the redox chemistry that can be performed by the transition metals is generally inaccessible. Parallels have been drawn between the chemistry of the group 2 complexes and that of trivalent and divalent lanthanides, due to their non-redox character and similarities in the ionic radii.<sup>70</sup> It has been shown that trivalent lanthanides generally react in two ways,  $\sigma$ -bond metathesis and the insertion of an unsaturated carbon-carbon or carbon-heteroatom bond into a Ln-X  $\sigma$ -bond (Scheme 45).<sup>71</sup> In the last decade this knowledge has been applied to the use of group 2 complexes in homogeneous catalysis.<sup>72</sup>



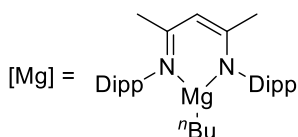
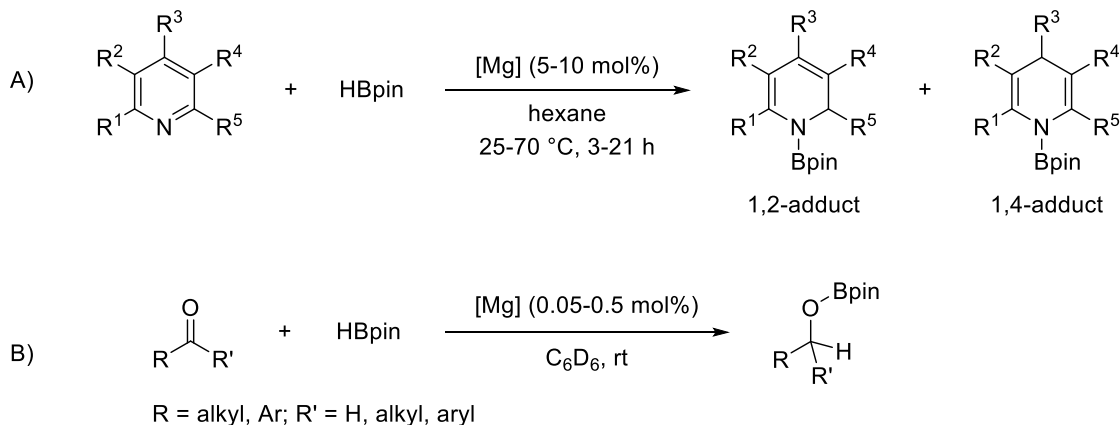
**Scheme 45:** Fundamental reactions of trivalent lanthanide complexes.

Organomagnesium chemistry has been well known and understood for the past 200 years.<sup>73</sup> There have been very few well characterised mono-alkyl and halide-free organomagnesium systems reported until recently, when a series of formally coordinatively unsaturated species were first reported using a bulky  $\beta$ -diketiminate ligand (Scheme 46).<sup>74</sup> It was shown that the reaction between group 2 complexes bearing this type of ligand and organosilanes selectively formed well-defined hydride species.<sup>75</sup> Using this method, dearomatisation of pyridine derivatives was reported. A successful catalytic protocol was not reported, however, as it was suggested that the strongly coordinating pyridine impeded interaction with the relatively non-basic phenylsilane and thus disfavoured the transition-state structure required for  $\sigma$ -bond metathesis.<sup>76</sup> In order to further develop this reaction, boronic esters were investigated as an alternative hydride source, which resulted in the successful hydroboration of pyridine and its derivatives (Scheme 47, A).<sup>77</sup> During this study, it was found that for substrates containing aldehyde and ester functionalities, addition across the C=O bond occurred exclusively. Following this, the magnesium-catalysed hydroboration of aldehydes and ketones were subsequently developed (Scheme 47, B).<sup>78</sup> Unsurprisingly, the reaction did not tolerate free

amines or alcohols, although no enolisation or aldol side reaction was seen for the ketone substrates as had been previously observed in the related calcium-catalysed hydrosilylation of ketones.<sup>79</sup>



**Scheme 46:** Mono-alkyl magnesium complexes with the  $\beta$ -diketiminato ligand.

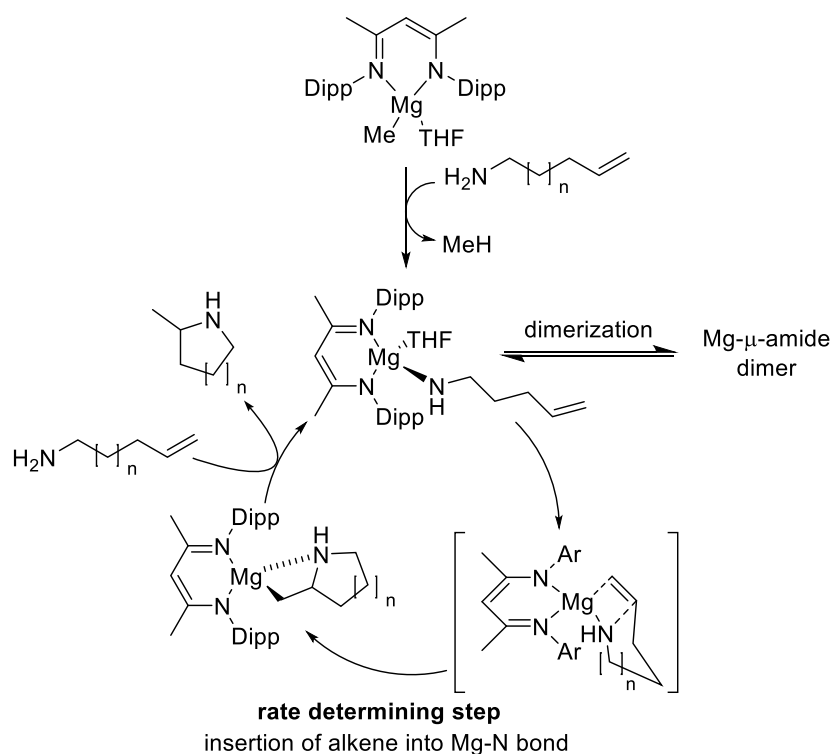


**Scheme 47:** Magnesium-catalysed hydroboration of pyridine derivatives, aldehydes and ketones.

Magnesium-catalysed reactions can also be achieved without the need for hydride sources, by using  $\sigma$ -bond metathesis to eliminate small molecules from a magnesium complex. Hill and co-workers reported the intramolecular hydroamination of aminoalkenes using several group 2 complexes including a methylmagnesium  $\beta$ -diketiminato complex.<sup>80</sup> In this reaction a non-reversible protonolysis would occur to form the magnesium amide complexes and an equivalent of methane gas. These amide complexes were then isolated and identified as the active catalysts. Mechanistic studies were conducted, and a mechanism

was proposed for magnesium-catalysed intramolecular hydroamination (Scheme 48), including a non-reversible catalyst initiation. In contrast, calcium complexes can react *via* a reversible catalyst initiation.<sup>81</sup> This was the first step towards hydrofunctionalisation of unsaturated carbon-carbon bonds rather than the more polarised unsaturated carbon-heteroatom bonds. In a subsequent publication, for the first time, an intermolecular hydroamination and tandem intramolecular/intermolecular hydroamination catalysed by a magnesium complex was demonstrated.<sup>82</sup>

There is great potential for the development of alkaline-earth metal catalysed hydrofunctionalisation, as demonstrated by recent publications. While hydroamination has been reported for alkene hydrofunctionalisation, other reactions such as hydroboration have been limited to unsaturated C=X bonds (where X = N or O). Alkene hydroboration is of great importance, as the boronic ester products of these reactions are key intermediates in the formation of various carbon-carbon and carbon-heteroatom bonds.<sup>18,83</sup> Therefore, an alkaline-earth metal catalysed alkene hydroboration would be highly valuable.

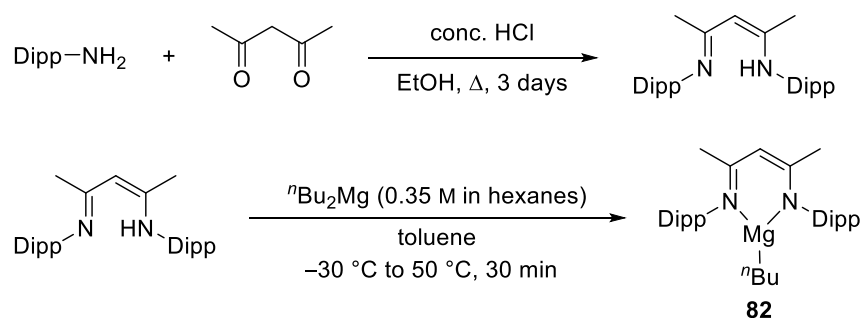


**Scheme 48:** Mechanism for magnesium-catalysed hydroamination.

## 3.2: Results and Discussion

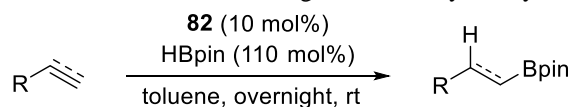
### 3.2.1: Olefin Hydroboration

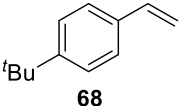
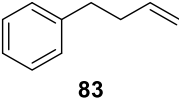
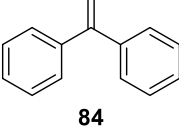
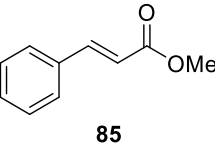
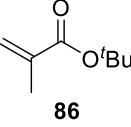
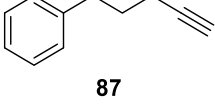
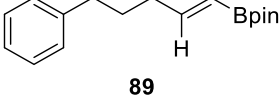
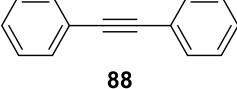
The magnesium complex **82** previously used by Hill and co-workers for the hydroboration of aldehydes and ketones was initially synthesised following literature procedures (Scheme 49).<sup>78</sup> Using this complex, an initial screen for the hydroboration of olefins in different environments was carried out in order to determine the viability of a possible carbon-carbon double bond hydrofunctionalisation using an alkaline-earth metal catalyst (Table 8). Unfortunately, no reaction was observed for a styrene derivative **68**, an alkyl alkene **83** or an activated 1,1-disubstituted alkene **84**, despite using a stoichiometric amount of **82** for the latter (Table 8, Entries 1-3). Alkenes **85** and **86**, containing ester functionalities, were also used in the hope that a slight polarisation of the carbon-carbon double bond may result in hydroboration, however this was also unsuccessful (Table 8, Entries 4 and 5). Upon switching from alkenes to an alkyl alkyne **87**, the (*E*)-vinylboronic ester **89** was found in a low yield (9%) (Table 8, Entry 6). This promising result demonstrated that alkyne hydroboration catalysed by an alkaline-earth metal was a potentially viable reaction. When a hindered, internal alkyne **88** was used, however, no product was observed once again (Table 8, Entry 7).



**Scheme 49:** Synthesis of magnesium complex **82** used in this work.



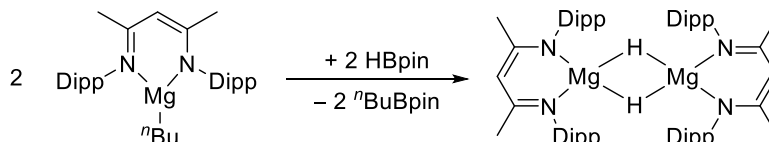
**Table 8:** Initial alkene screen for magnesium-catalysed hydroboration.

Entry <sup>a</sup>	Alkene	Product	Yield (%) <sup>b</sup>
1	 <b>68</b>	n/a	0
2	 <b>83</b>	n/a	0
3 <sup>c</sup>	 <b>84</b>	n/a	0
4	 <b>85</b>	n/a	0
5	 <b>86</b>	n/a	0
6	 <b>87</b>	 <b>89</b>	9 <sup>b</sup>
7	 <b>88</b>	n/a	0

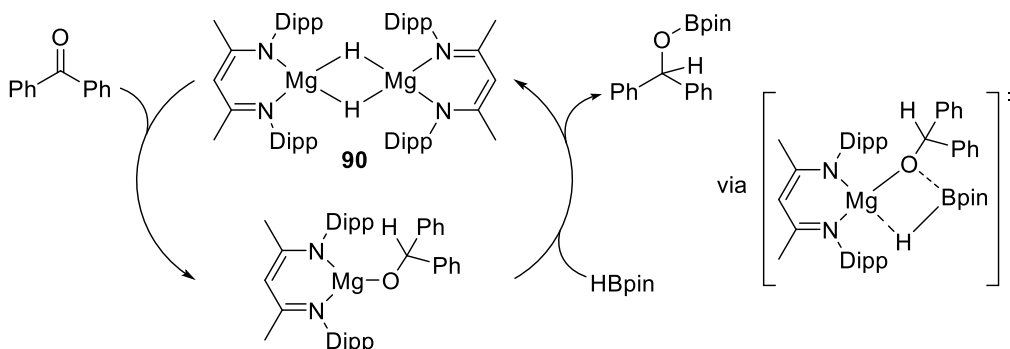
<sup>a</sup> Olefin (2 mmol), **82** (10 mol%) and HBpin (2.05 mmol). <sup>b</sup> Yield determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene (20 mol%) as internal standard. <sup>c</sup> Alkene 0.4 mmol, **82** (0.4 mmol), HBpin (0.8 mmol).

A control reaction using just dibutylmagnesium in the absence of ligand showed that there was some background reactivity, although only 3% of the vinyl boronic ester **89** was observed in the <sup>1</sup>H NMR spectra. Analysis of the <sup>11</sup>B NMR spectra, however, did reveal that the 1-butylboronic acid pinacol ester had been formed (singlet at 22.2 ppm), along with some small quantities of BH<sub>3</sub> (quartet at -15 ppm). These results are consistent with the σ-bond metathesis mechanism proposed by Hill and co-workers (Schemes 50 and 51), although the presence of a small amount of BH<sub>3</sub> could potentially allude to a decomposition of the HBpin as has been observed previously for titanium “catalysed” hydroboration.<sup>84</sup> In this case, it was shown that reported titanium-catalysed processes were causing catechol borane to decompose to BH<sub>3</sub>, which was then able to perform an uncatalysed hydroboration. In the absence of magnesium, there was no reaction at

all, demonstrating the requirement of the magnesium complex for hydroboration to take place.



**Scheme 50:** Activation of magnesium complex by pinacol borane.

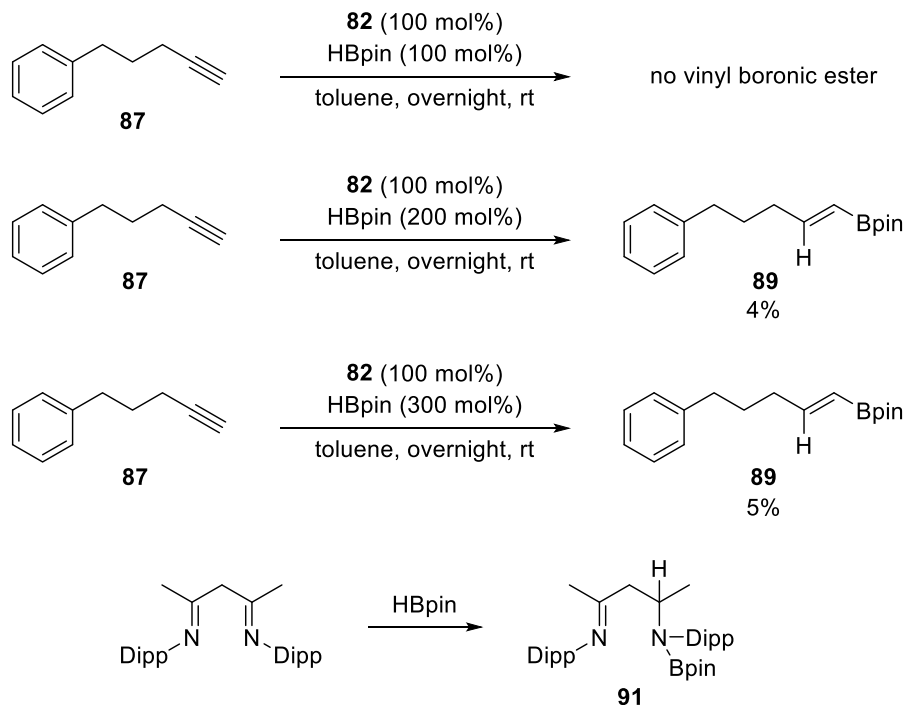


**Scheme 51:** Proposed catalytic cycle for the hydroboration of ketones.

It was proposed that a more activated alkyne may have a higher propensity for reaction with the magnesium complex, and so the addition of silver triflate as a  $\pi$ -acid additive was attempted. This was, however, unsuccessful in improving the yield of product any further (4% of the vinyl boronic ester **89** was observed by  $^1\text{H}$  NMR). Although the donation of electrons from the  $\pi$ -acid into the anti-bonding orbitals of the alkyne would have weakened the carbon-carbon bond, it also results in a more electron-rich system which may have hindered nucleophilic attack of the putative “hydride” complex **90**, presumably generated *in situ*, on the alkyne.

As the best result gave just a 9% yield of the vinylboronic ester (Table 8, Entry 6), several reactions using stoichiometric loadings of magnesium complex **82** with varying amounts of pinacol borane were carried out (Scheme 52). Using a 1:1 mixture of magnesium complex **82** and pinacol borane did not result in any of the vinyl boronic ester **89**, however the 1-butylboronic acid pinacol ester was detected in the  $^{11}\text{B}$  NMR spectra (singlet at 22.2 ppm) and another peak was detected at 43.4 ppm. This peak is too far upfield, however, for a potential trivinyl species that may form from a hydroboration reaction with  $\text{BH}_3$ .<sup>85</sup> It could be tentatively assigned to a trialkynyl species, although it is not completely clear how this species would form under the current conditions. Using two equivalents of pinacol borane resulted in a small amount of the vinyl boronic ester **89** being formed, but there was no improvement on previous results. Analysis of the  $^1\text{H}$  NMR spectra also showed that there were two septets for the *isopropyl* groups in the ligand. This suggests that the two sides of the ligand are non-equivalent, which may be the result of a desymmetrisation between pinacol borane and the ligand to give **91**. As a stoichiometric amount of complex is present in

these reactions, a preferential reaction with the carbon-nitrogen bond may be taking place over any potential reaction with a non-polarised carbon-carbon unsaturated system. The reaction with three equivalents of pinacol borane gave similar results to the reaction using two equivalents.

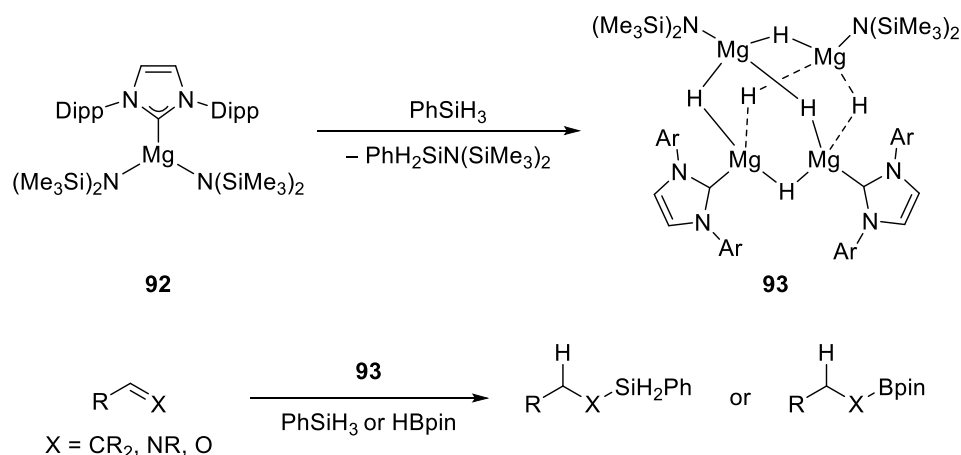


**Scheme 52:** Hydroboration reactions using stoichiometric amounts of the magnesium  $\beta$ -diketiminato complex and the potential ligand desymmetrisation reaction.

The method did not appear to be making any progress even using stoichiometric amounts of magnesium complex, and was moving further away from the operational simplicity that was set as a broad aim of the project so other avenues of research were pursued.

### 3.2.2: Ketone Hydrosilylation and Hydroboration

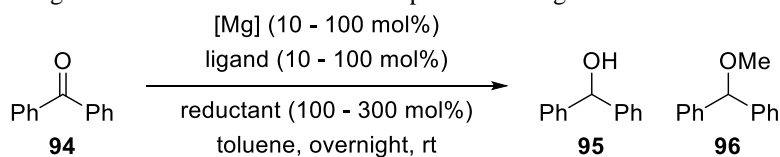
Hill and co-workers reported an NHC magnesium complex **92** that when treated with phenylsilane produced a magnesium hydride cluster **93**.<sup>86</sup> It was proposed that this cluster may be used to deliver hydride to an appropriate acceptor and thus enable a hydrofunctionalisation of an unsaturated system (Scheme 53).



**Scheme 53:** Generation of a magnesium-hydride cluster and potential use for hydrofunctionalisation.

As carbonyls are more polarised than carbon-carbon double bonds, carbonyl reduction was initially targeted using benzophenone **94** as a model substrate for the initial screening studies (Table 9). Using a 10 mol% loading of the pre-formed NHC complex **92** as catalyst resulted in a 10% yield of alcohol **95**, although it was unclear whether the magnesium hydride cluster **93** was formed under these conditions (Table 9, Entry 1). As this appeared to be a stoichiometric conversion to product with respect to catalyst, a reaction was run using a mixture of the magnesium salt and free carbene ligand, using a 100 mol% loading for both reagents. This gave alcohol **95** in an 85% yield (Table 9, Entry 2). It was assumed that the magnesium salt and ligand would form a complex *in situ*, nevertheless it was important to determine whether there was any reactivity with either the magnesium salt or free ligand. In the absence of ligand, the reaction of  $[\text{Mg}(\text{HMDS})_2]$  with benzophenone and phenylsilane gave alcohol **95** in a 23% yield demonstrating some reactivity with the magnesium salt alone (Table 9, Entry 3). An alternative reductant was also investigated; phenylsilane was substituted with HBpin in a reaction with  $\text{Mg}(\text{HMDS})_2$  in the absence of any ligand, which resulted in a 78% yield of alcohol **95** (Table 9, Entry 4). This indicates a significant reaction between the magnesium salt and pinacol borane. Reactions in the absence of any alkaline-earth metal salt or ligand were unsuccessful returning only starting material (Table 9, Entries 5 and 6). When the catalyst loading was reduced back down to 10 mol%, the reaction with phenylsilane proceeded to give a 12% yield of alcohol **95** whereas the reaction with pinacol borane gave an overall conversion to product of 97% (Table 9, Entries 7 and 8). The reaction with pinacol borane gave a mixture of alcohol **95** and methyl ether **96**, presumably formed by the elimination of water under acidic conditions and the subsequent reaction with methanol (Scheme 54). This result suggested that the hydroboration of benzophenone could be catalysed with  $\text{Mg}(\text{HMDS})_2$  salt alone. Other HMDS salts were investigated to determine whether the reaction was base catalysed or whether there was a genuine interaction with magnesium metal. Both  $\text{NaHMDS}$  and  $\text{KHMDS}$  gave similar results to the magnesium salt when using phenylsilane as reductant, with yields of 20% and

14% of alcohol **95** respectively (Table 9, Entries 9 and 11). As with  $\text{Mg}(\text{HMDS})_2$ , the reactions using  $\text{NaHMDS}$  and  $\text{KHMDS}$  with pinacol borane also gave high conversions to product, with overall conversions of 84% and 87% respectively (Table 9, Entries 10 and 12). As there had been only a minor background reaction with the metal salts and phenylsilane, the reaction with the free carbene was also investigated. Alcohol **95** was observed in an 80% yield, demonstrating the capability of the carbene to mediate a reduction of the benzophenone by itself (Table 9, Entry 13). Although an NHC-mediated hydrosilylation of ketones has not been reported previously, it is not a surprising result given the reactivity of NHCs already known.<sup>87</sup>

**Table 9:** Investigation into the reduction of benzophenone using an alkaline-earth metal catalyst.

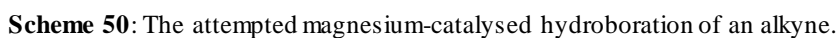
Entry	[Mg] (x mol%)	Ligand (x mol%)	Reductant <sup>a, b</sup> (x mol%)	Yield of 95 <sup>c</sup> (%)	Yield of 96 <sup>c</sup> (%)
1	 (10)	-	PhSiH <sub>3</sub> (130)	9	-
2	Mg[N(SiMe <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> (100)	 (100)	PhSiH <sub>3</sub> (300)	85	-
3	Mg[N(SiMe <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> (100)	-	PhSiH <sub>3</sub> (300)	23	-
4	Mg[N(SiMe <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> (100)	-	HBpin (100)	78	-
5	-	-	PhSiH <sub>3</sub> (300)	-	-
6	-	-	HBpin (100)	-	-
7	Mg[N(SiMe <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> (10)	-	PhSiH <sub>3</sub> (110)	12	-
8	Mg[N(SiMe <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> (10)	-	HBpin (100)	30	67
9	NaN(SiMe <sub>3</sub> ) <sub>2</sub> (10)	-	PhSiH <sub>3</sub> (110)	20	-
10	NaN(SiMe <sub>3</sub> ) <sub>2</sub> (10)	-	HBpin (100)	38	46
11	KN(SiMe <sub>3</sub> ) <sub>2</sub> (10)	-	PhSiH <sub>3</sub> (110)	14	-
12	KN(SiMe <sub>3</sub> ) <sub>2</sub> (10)	-	HBpin (100)	17	70
13	-	 (100)	PhSiH <sub>3</sub> (300)	80	-

<sup>a</sup>Work-up method A (see Experimental, Section 6.4.1) was used for all reactions with PhSiH<sub>3</sub>. <sup>b</sup>Work-up method B (see Experimental, Section 6.4.1, p. 103) was used for all reactions with HBpin. <sup>c</sup>Determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard.

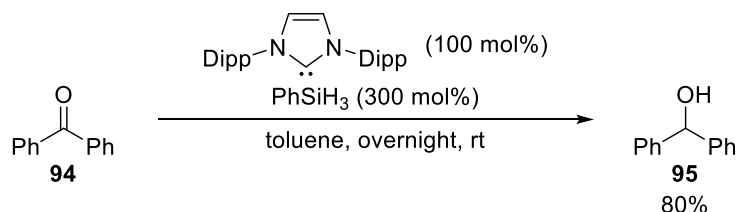


### 3.3: Conclusions and Future Work

The hydroboration of olefins using a well-defined magnesium complex was attempted using a previously reported complex that had been successful in catalysing several reactions, including alkene hydroamination. Unfortunately, there was very limited success for hydroboration with the only result coming from a reaction with 5-phenyl-1-pentyne to give the (*E*)-vinylboronic ester product **89** in a low yield (Scheme 50). Running reactions with a stoichiometric amount of the magnesium complex did not improve the yield any further and so it was presumed that either a reaction with the ligand prevented the stoichiometric reaction from proceeding or that the low yield was resulting from a background reaction in the first place. The presence of BH<sub>3</sub> in the <sup>11</sup>B NMR spectra of some of the reactions suggests that perhaps a small amount of BH<sub>3</sub> is formed under reaction conditions which may result in catalyst-free hydroboration.



45



**Scheme 51:** The hydrosilylation of benzophenone mediated by an *N*-heterocyclic carbene.

The hydroboration of benzophenone was observed to occur with different amide salts to give a mixture of alcohol and ether products. While this has also been unreported in the literature, the base-catalysed reduction of esters, ketones and aldehydes using silanes has been reported.<sup>89</sup>

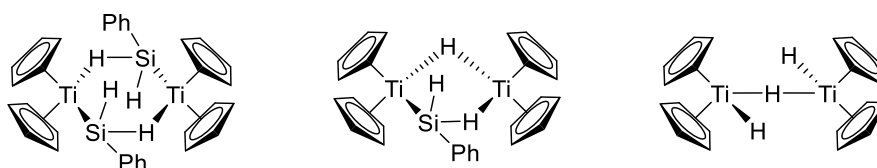
It would be interesting to carry out mechanistic studies to determine whether borane is being formed *in situ* upon mixing of pinacol borane and the  $\beta$ -diketiminate *n*-butylmagnesium complex, although it is likely that contaminated starting material may have contained small amounts of  $\text{BH}_3$ . Further studies could also include the investigation into the interaction between amide salts and pinacol borane. The formation of hypervalent boronate species is well documented so it would be possible to determine whether such a species is forming under the reaction conditions. A similar reaction has recently been published using a lanthanide amide salt,<sup>90</sup> and as comparisons have been drawn previously between the group 2 metals and lanthanides, it would be interesting to see the results of their further mechanistic studies.



## Chapter 4: Titanium-Catalysed Hydrogenation and Hydrosilylation of Olefins

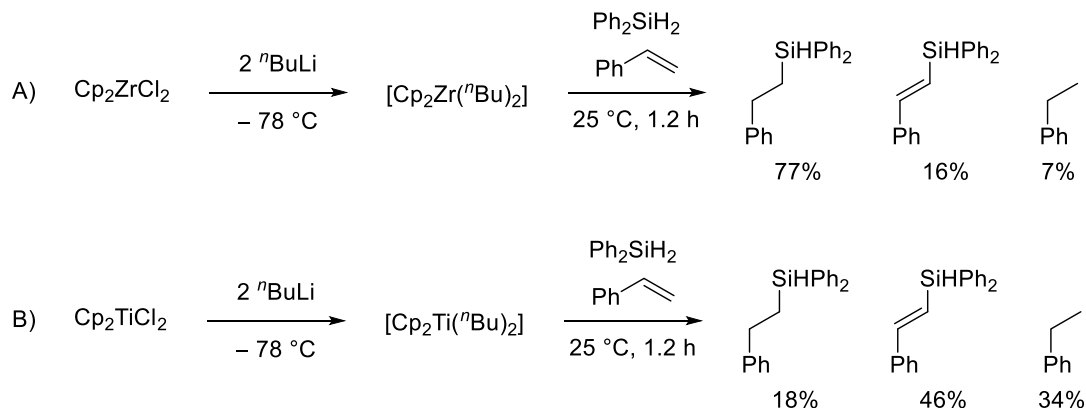
### 4.1: Introduction

In contrast to group 8, 9 and 10 transition metals, the early transition metals, such as titanium, have not seen the same development in catalysed olefin hydrosilylation. The first example of a titanium-catalysed hydrosilylation came from an investigation into the reaction intermediates of a dehydrogenative coupling of organosilanes using dimethyl titanocene,  $\text{Cp}_2\text{TiMe}_2$ .<sup>91</sup> Three complexes were identified from spectroscopic data as being involved in the polymerisation reaction of primary organosilanes (Figure 2). When an attempt to perform a dehydrogenative coupling in the presence of an alkene was made, however, hydrogenation of the carbon-carbon double bond took place. Throughout the substrate scope, hydrogenation remained the dominant reaction but low yields of hydrosilylation were observed for alkyl alkenes (including internal alkenes), norbornene and styrene. The rate of the reaction was observed to be several magnitudes higher when norbornene and styrene were used in comparison to the other substrates.



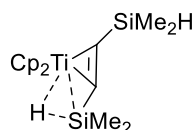
**Figure 2:** Three complexes observed as intermediates in the  $\text{Cp}_2\text{TiMe}_2$ -catalysed polymerisation of organosilanes.

Early reports on group 4 transition-metal-catalysed olefin hydrosilylation focused on zirconium catalysts. When used in combination with either Grignard reagents or organolithium species, catalytically active zirconium species could be generated for the anti-Markovnikov selective hydrosilylation of terminal alkenes (Scheme 52, A).<sup>92</sup> It was later found that simply by changing the relative ratio of organolithium to zirconium pre-catalyst, the selectivity could be reversed for styrene derivatives to give the Markovnikov addition product.<sup>93</sup> Titanium catalysts were also tested, however the chemoselectivity was reduced in comparison to the analogous reactions using zirconium catalysts and a greater distribution of products was formed (Scheme 52, B).<sup>92b</sup>

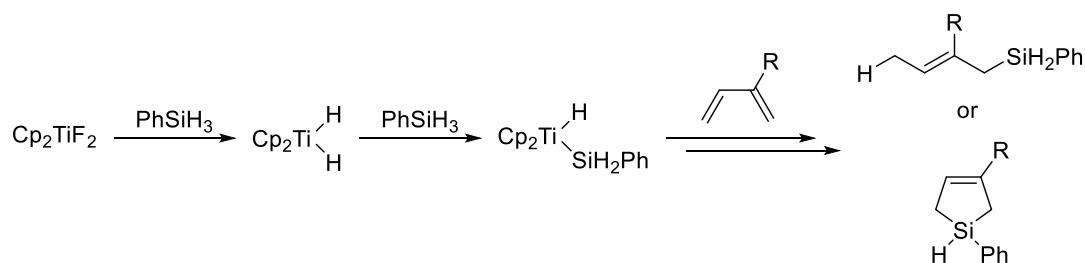


**Scheme 52:** An example of the anti-Markovnikov selective hydrosilylation of terminal alkenes using a zirconium pre-catalyst.

A *syn*-selective hydrosilylation of alkynes was reported by Takahashi *et al.*<sup>94</sup> using conditions previously reported for titanium-catalysed hydrosilylation by the groups of Corey and Waymouth.<sup>92b,92c</sup> In this case,  $\text{Cp}_2\text{TiCl}_2$  was reacted with  $^n\text{BuLi}$  to produce a catalytically-active species. Unlike the previous reports, only the hydrosilylation products were isolated in high yields and with high regioselectivity. The substrate scope was limited to alkyl alkynes, although both terminal and internal alkynes underwent successful hydrosilylation. An  $\eta^2$ -alkyne complex of titanocene had been previously reported,<sup>95</sup> and it was suggested that the mechanism for the reaction could feasibly proceed through a similar intermediate. The X-ray crystal structure of this  $\eta^2$ -complex shows a drastic bend of the Si-H bond towards the metal centre (Figure 3), and it may be that this interaction gives rise to the regioselectivity in this case. More recently, the first titanium-catalysed *anti*-1,4-hydrosilylation of dienes was reported using titanocene difluoride,  $\text{Cp}_2\text{TiF}_2$  as the pre-catalyst.<sup>96</sup> A variety of dienes and silanes were compatible with reaction conditions giving the allylsilane products in moderate to excellent yields. By activating the pre-catalyst in the absence of diene, dehydrogenative silylation products were also able to be observed. The reaction was proposed to proceed through a silyltitanium hydride species, presumably formed *via* a titanium-dihydride species that results from a  $\sigma$ -bond metathesis reaction between titanocene difluoride and phenylsilane (Scheme 53).



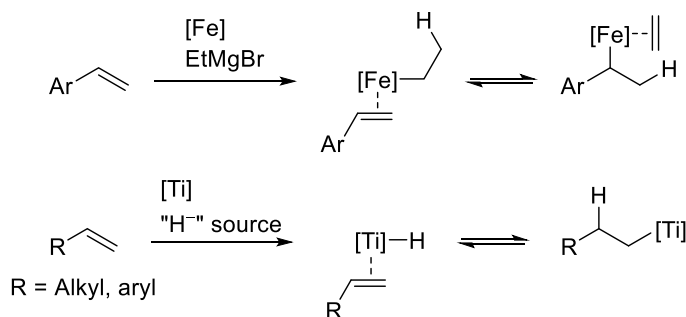
**Figure 3:** Significant Si-H-Ti interaction in the  $\eta^2$ -titanocene alkyne complex.



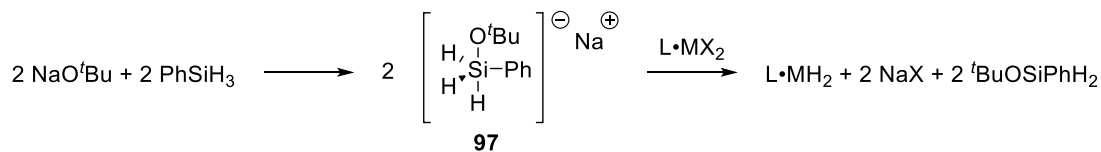
**Scheme 53:** Generation of silyltitanium hydride species in the titanium-catalysed 1,4-hydrosilylation of 1,3-dienes.

## 4.2: Results & Discussion

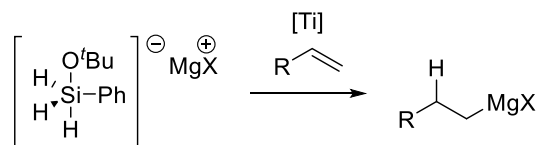
This project began as an attempt to increase the scope of catalytic hydromagnesiation reactions. As titanium-catalysed hydromagnesiation had previously been proposed to occur through a titanium-hydride intermediate,<sup>47</sup> it was thought that this may enable the functionalisation of carbon-carbon double bonds that the iron-catalysed system was incapable of carrying out (Scheme 54). In order to establish a novel method of generating titanium-hydride species, the hypervalent silicon “ate” species **97**, used within the group previously for the activation of transition metal catalysts,<sup>42</sup> was investigated. These reactive species could be generated *in situ* by reacting an organosilane, such as phenylsilane, with sodium *tert*-butoxide and then reacted with the metal pre-catalyst to form “active” metal-hydride species (Scheme 55). It was envisaged that using titanium, together with an alkoxy magnesium salt and phenylsilane, a titanium hydride species could be generated under mild conditions and then a transmetalation could occur with magnesium to form a Grignard reagent (Scheme 56).



**Scheme 54:** Differing hydrometallation mechanisms between iron and titanium catalysts.



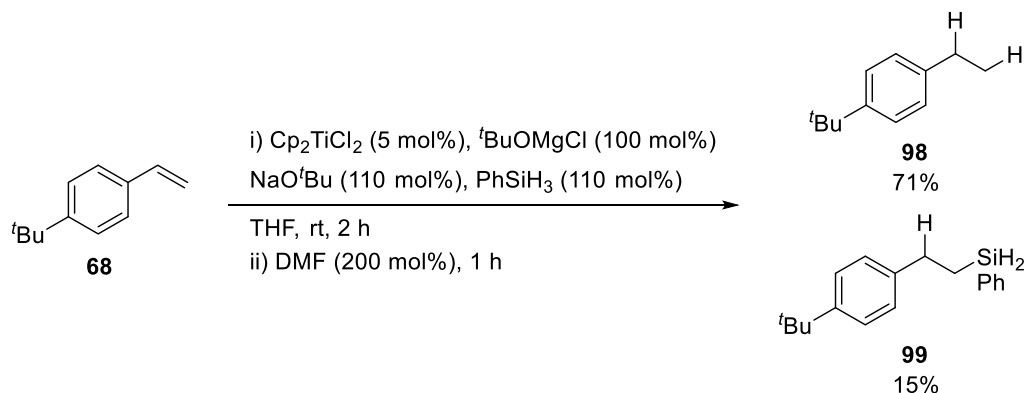
**Scheme 55:** Generation of a hypervalent silicon “ate” species for the activation of metal complexes.



**Scheme 56:** Formation of a Grignard reagent using titanium and a silicon “ate” species.

### 4.2.1: Initial Screening Reactions

Initial reactions used the magnesium salt  $t\text{BuOMgCl}$  as it had been reported to be soluble in THF previously,<sup>97</sup> however the hydrogenation product **98** was observed in a 71% yield and the hydrosilylation product **99** was observed in a 15% yield rather than any product of a hydromagnesiation reaction (Scheme 57). From this result, it was unclear whether any hydromagnesiation had occurred or not, as the hydrogenation product could have resulted from a Grignard reagent reacting with a proton source.

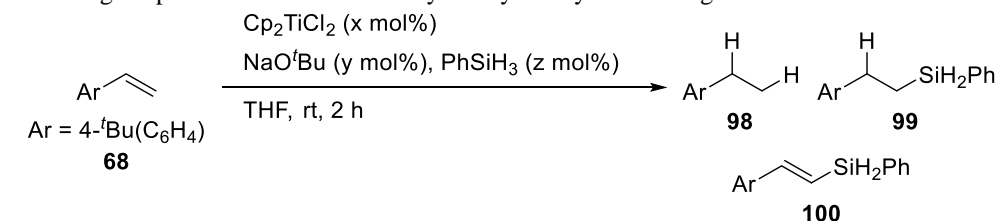


**Scheme 57:** Attempted titanium-catalysed hydromagnesiation using sodium *tert*-butoxide as a catalyst activator.

A series of reactions were then performed in the absence of magnesium to assess the potential for a titanium-catalysed hydrosilylation reaction and to determine whether or not product **98** was formed *via* a reactive organomagnesium species (Table 10). An equivalent reaction, albeit without any magnesium salt, resulted in the formation of product **98** in a 50% yield (Table 10, Entry 1). Increasing the loading of pre-catalyst and the activating mixture (sodium *tert*-butoxide and phenylsilane) gave a slight increase in the yield of product **98**, up to 62% (Table 10, Entry 2). In both cases, no product **99** was observed. Reducing the amount of sodium *tert*-butoxide activator to a sub-stoichiometric amount, in line with the studies reported by Docherty and co-workers<sup>42</sup> resulted in the formation of both hydrogenation and hydrosilylation products, **98** and **99**, in a 42% and 35% yield, respectively (Table 10, Entry 3). The presumed dehydrogenative silylation product **100** was also formed in low yield (17%). Upon oxidation of the reaction mixture, a mixture of alcohol **101** and aldehyde **102** was observed, thus confirming the presence of a vinyl silane (Scheme 58). Different

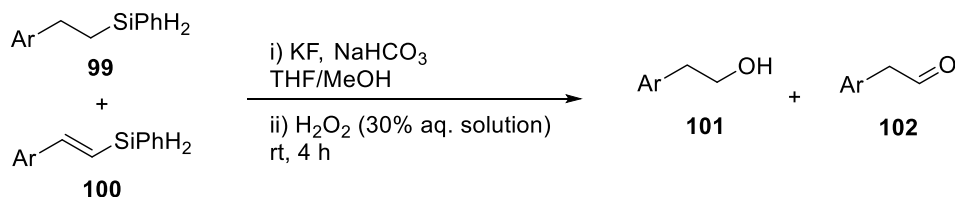
activators were then investigated, however the use of metal fluorides proved unsuccessful which may suggest that the reactive silicon-“ate” species is unable to be formed with a nucleophilic fluoride in this system (Table 10, Entries 4 and 5). Potassium *tert*-butoxide gave similar results to the reaction with sodium *tert*-butoxide, demonstrating that the counter ion has little effect on the outcome of the reaction (Table 10, Entry 6). A control reaction was performed in the absence of any *tert*-butoxide salt or other activator, returning only starting material and thus eliminating any potential background reaction between phenylsilane and titanocene dichloride (Table 10, Entry 7).

**Table 10:** Assessing the potential of titanium-catalysed hydrosilylation using NaO<sup>t</sup>Bu as an activator.



Entry	Cp <sub>2</sub> TiCl <sub>2</sub> (x mol%)	NaO <sup>t</sup> Bu (y mol%)	PhSiH <sub>3</sub> (z mol%)	98 (%)	99 (%)	100 (%)
1	5	110	110	50	-	-
2	100	200	300	62	-	-
3	5	10	110	42	35	17
4 <sup>a</sup>	5	-	110	-	-	-
5 <sup>b</sup>	5	-	110	-	-	-
6 <sup>c</sup>	5	-	110	41	40	13
7	5	-	100	-	-	-

<sup>a</sup> KF (10 mol%) was used, <sup>b</sup> NaF (10 mol%) was used, <sup>c</sup> KO<sup>t</sup>Bu (10 mol%) was used.



**Scheme 58:** Tamao oxidation of the mixture of silanes formed from titanium-catalysed reaction.

## 4.2.2: Substrate Scope

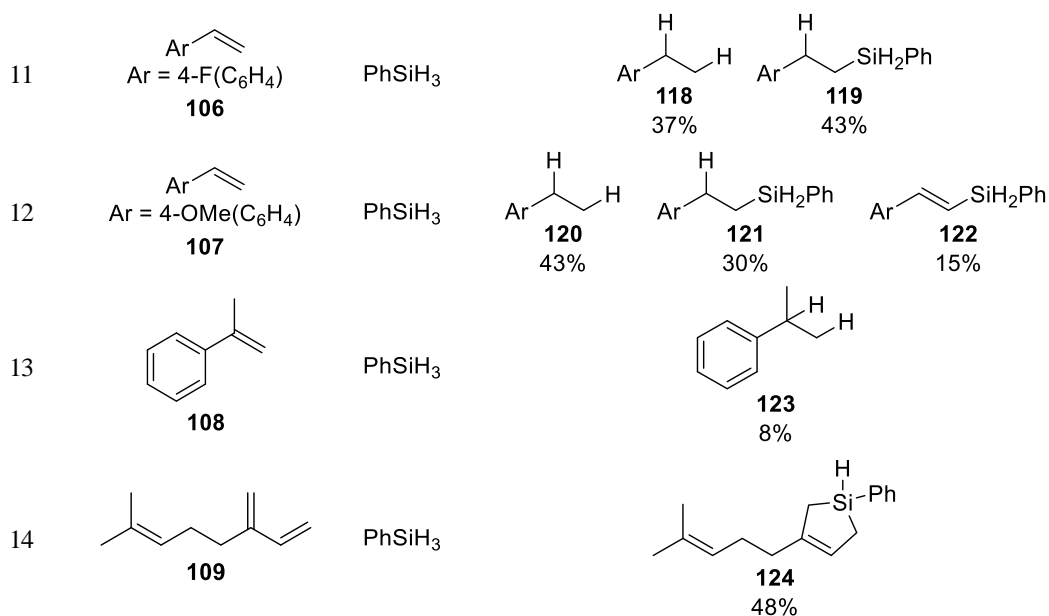
Screening of other organosilanes and olefin substrates then took place to determine whether any other silanes had greater reactivity, and whether the substrate scope could be expanding to other olefins (Table 11). Interestingly, replacing phenylsilane with triethoxysilane gave only hydrogenation product **98** from 4-

*tert*-butylstyrene **68** in a moderate yield (55%) and when diphenylsilane was used no reaction took place (Table 11, Entries 1 and 2). This may be due to a rapid disproportionation of triethoxysilane in the presence of sodium *tert*-butoxide to give SiH<sub>4</sub>, although none of the crude reaction mixtures appeared to have the pyrophoric nature that is normally associated with SiH<sub>4</sub>. Formation of the silicon-“ate” complex using diphenylsilane may be slower or the reaction with the titanium complex may not be energetically favourable. The attempted reaction with 4-phenylbutene **83** resulted in only low yields of the hydrogenation product **110**, with phenylsilane giving the highest yield (25%) and diphenylsilane the lowest (4%) (Table 11, Entries 3-5). When oct-1-ene **103** was used, no hydrogenation or hydrosilylation products were observed, and only starting material and the isomerisation product, oct-4-ene **111**, were detected by <sup>1</sup>H NMR spectroscopy (Table 11, Entries 6 and 7). It is possible that some hydrogenation took place and the volatile product was lost on work-up, however this cannot be confirmed. Two terminal alkynes, 5-phenyl-1-pentyne **87** and phenylacetylene **104**, were also investigated. In the case of 5-phenyl-1-pentyne, the alkyne underwent a double reduction to give the alkylsilane product **112** in 18% yield (Table 11, Entry 8). This presumably occurs *via* a hydrosilylation/hydrogenation tandem reaction, although with the absence of any alkene or vinylsilane in the crude reaction mixture it is not possible to determine which reaction occurs first. The reaction with phenylacetylene gave a mixture of hydrogenation, hydrosilylation and reduced hydrosilylation products (**69**, **113** and **114** respectively) albeit in low yields (Table 11, Entry 9). Electronically differentiated styrene derivatives were investigated next to determine if there was any impact on product distribution. The use of a styrene bearing a strongly electron-withdrawing CF<sub>3</sub> group, **105**, resulted in moderate yields of the hydrogenation and hydrosilylation products, **115** and **116** (42% and 32%, respectively), and a slightly lower yield of dehydrogenative silylation product **117** (22%) (Table 11, Entry 10). The more electron neutral 4-fluorostyrene **106** did not undergo a dehydrogenative silylation reaction, however moderate yields of the hydrogenation and hydrosilylation products **118** and **119** were observed (Table 11, Entry 11). A styrene derivative bearing an electron-donating group, 4-methoxystyrene **107**, gave similar results to that of 4-trifluoromethylstyrene with hydrogenation, hydrosilylation and dehydrogenative silylation products, **120**, **121** and **122** being observed in 43%, 30% and 15% yield, respectively (Table 11, Entry 12). This result suggests that the electronics of the substrate have very little effect on the course of the reaction.  $\alpha$ -Methylstyrene **108** was investigated to determine whether 1,1-disubstituted alkenes were compatible with the reaction. Unfortunately, the only product observed was the hydrogenation product **123** in a very low yield (8%) (Table 11, Entry 13). Lastly, as a 1,4-hydrosilylation of 1,3-dienes had been reported in the literature previously using titanocene difluoride,<sup>96</sup> myrcene **109** was subject to the reaction conditions in order to determine whether it would react in a similar manner to that previously reported (Table 11, Entry 14). Although no hydrosilylation was observed, the cyclic silylation product **124** was detected in a moderate 48% yield. This product was also reported by Möise *et. al.* when the pre-catalyst

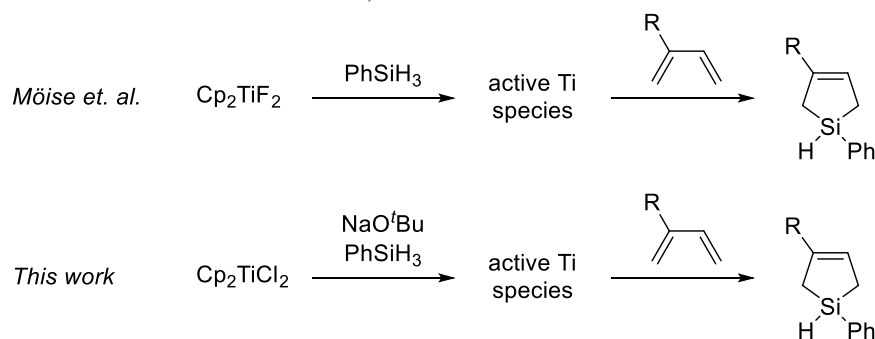
was activated with phenylsilane in the absence of the diene substrate,<sup>96</sup> similar to how the catalyst is activated under the current reaction conditions (Scheme 59). In the work of Möise and co-workers, when the catalyst is activated in the presence of the diene then the 1,4-hydrosilylation product is the major product.

**Table 11:** Olefin and silane scope in the titanium-catalysed hydrosilylation reaction.

$\text{R}-\text{C}\equiv\text{C} \xrightarrow[\text{THF, rt}]{\text{Cp}_2\text{TiCl}_2 (5 \text{ mol\%}), \text{NaO}^t\text{Bu} (10 \text{ mol\%}), \text{R}_3\text{SiH} (110 \text{ mol\%})} \text{products}$			
Entry <sup>a,b</sup>	Olefin	Silane	Product
1	$\text{Ar}-\text{CH}=\text{CH}_2$ $\text{Ar} = 4\text{-}^t\text{Bu}(\text{C}_6\text{H}_4)$ <b>68</b>	(EtO) <sub>3</sub> SiH	$\text{Ar}-\text{CH}_2\text{CH}_2\text{H}$ <b>98</b> 55%
2	$\text{Ar}-\text{CH}=\text{CH}_2$ $\text{Ar} = 4\text{-}^t\text{Bu}(\text{C}_6\text{H}_4)$ <b>68</b>	Ph <sub>2</sub> SiH <sub>2</sub>	-
3	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$ <b>83</b>	PhSiH <sub>3</sub>	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{H}$ <b>110</b> 25%
4	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$ <b>83</b>	(EtO) <sub>3</sub> SiH	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{H}$ <b>110</b> 10%
5	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$ <b>83</b>	Ph <sub>2</sub> SiH <sub>2</sub>	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{H}$ <b>110</b> 4%
6	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CH}_2$ <b>103</b>	PhSiH <sub>3</sub>	$\text{C}_3\text{H}_7-\text{CH}=\text{CH}-\text{C}_3\text{H}_7$ <b>111</b> 16%
7	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CH}_2$ <b>103</b>	(EtO) <sub>3</sub> SiH	$\text{C}_3\text{H}_7-\text{CH}=\text{CH}-\text{C}_3\text{H}_7$ <b>111</b> 19%
8	$\text{Ph}-\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{CH}$ <b>87</b>	PhSiH <sub>3</sub>	$\text{Ph}-\text{CH}_2(\text{CH}_2)_3\text{SiH}_2\text{Ph}$ <b>112</b> 18%
9	$\text{Ph}-\text{C}\equiv\text{C}-\text{H}$ <b>104</b>	PhSiH <sub>3</sub>	$\text{Ph}-\text{CH}=\text{CH}_2$ <b>69</b> 5% $\text{Ph}-\text{CH}=\text{CH}-\text{SiH}_2\text{Ph}$ <b>113</b> 15% $\text{Ph}-\text{CH}_2\text{CH}_2\text{SiH}_2\text{Ph}$ <b>114</b> 3%
10	$\text{Ar}-\text{CH}=\text{CH}_2$ $\text{Ar} = 4\text{-CF}_3(\text{C}_6\text{H}_4)$ <b>105</b>	PhSiH <sub>3</sub>	$\text{Ar}-\text{CH}_2\text{CH}_2\text{H}$ <b>115</b> 42% $\text{Ar}-\text{CH}_2\text{CH}_2\text{SiH}_2\text{Ph}$ <b>116</b> 32% $\text{Ar}-\text{CH}=\text{CH}-\text{SiH}_2\text{Ph}$ <b>117</b> 22%



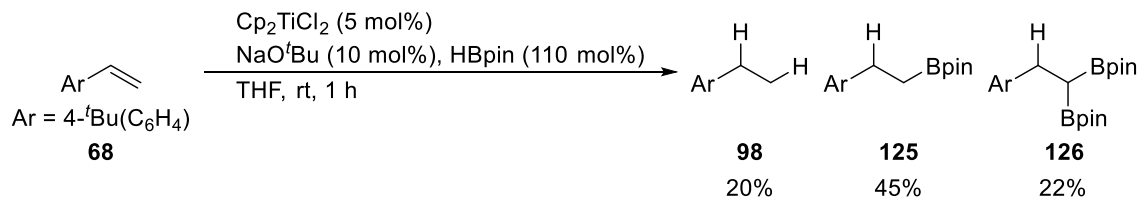
<sup>a</sup>All yields determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. <sup>b</sup>Entries 1-7 were run for 3 h, entries 8-14 were run for 1 h.



**Scheme 59:** Comparison between the methods discussed in this thesis and the work by Möise *et. al.*

The current method of catalyst activation has also previously been applied to hydroboration and so a titanium-catalysed hydroboration reaction was also attempted to see if there would be any difference in reactivity to hydrosilylation (Scheme 60). As with organosilanes, a mixture of products was observed on the attempted titanium-catalysed hydroboration of 4-*tert*-butylstyrene **68**, however the linear hydroboration product **125** was the major product of this reaction, observed in a 45% yield. Interestingly, alongside the hydrogenation by-product **98**, the geminal diboration product **126** was also observed in a 22% yield. The observation of this product strongly suggests that the reaction proceeds through a dehydrogenative boration and the vinyl boronic ester intermediate is then able to undergo hydroboration, however no vinyl boronic ester was detected in the crude reaction mixture by <sup>1</sup>H NMR spectroscopy or by GC-MS analysis.



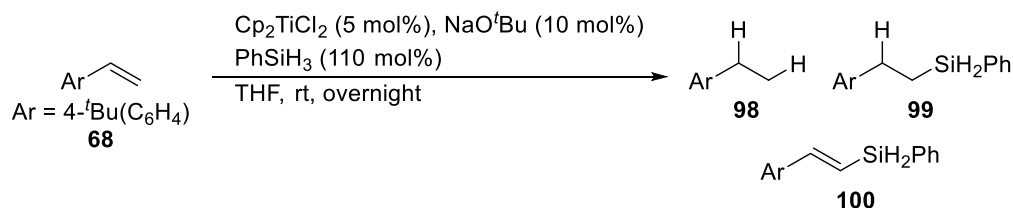


**Scheme 60:** Titanium-catalysed hydroboration of 4-*tert*-butylstyrene using sodium *tert*-butoxide as an activator.

### 4.2.3: Further Screening and Development

As changing the substrate did not give any significant results in terms of changing the product distribution, the reaction concentration was then investigated (Table 12). More concentrated reactions appeared to favour hydrogenation product **98**, whereas the hydrosilylation reaction appeared to perform better at lower concentrations of phenylsilane (Table 12, Entries 1 – 4). The dehydrogenative silylation product **100** was found to form only under the reaction conditions used previously, the most dilute reaction in this case (Table 12, Entry 5). A reaction in the absence of solvent proceeded in a similar fashion to reactions at higher concentration reactions (Table 12, Entry 6).

**Table 12:** Investigating the effect of reaction concentration on product distribution.



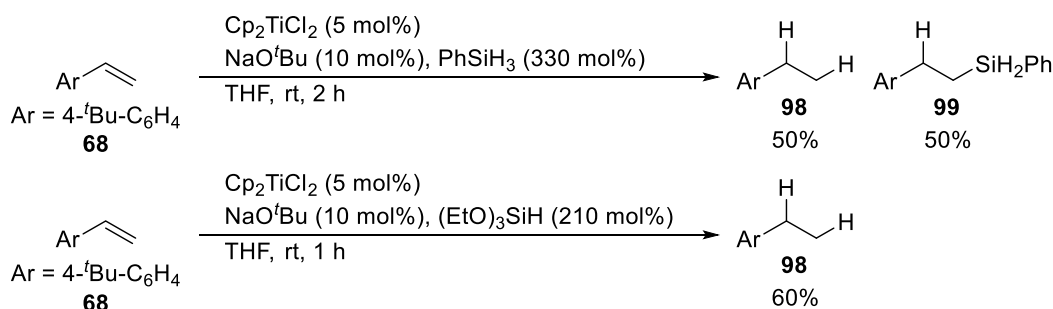
Entry <sup>a</sup>	Conc. of PhSiH <sub>3</sub> (mol L <sup>-1</sup> )	98 (%)	99 (%)	100 (%)
1	1.54	50	25	-
2	0.77	40	40	-
3	0.39	45	45	-
4	0.26	45	40	-
5	0.15	45	30	16
6	-	47	27	-

<sup>a</sup>All yields determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

Performing a reaction in neat triethoxysilane resulted exclusively in the formation of hydrogenation product **97** in 60% yield. This result is comparable to the same reaction with triethoxysilane run in solvent (Table 11, Entry 1) and thus it is clear that silane choice has a significant impact on the outcome of the reaction.

The choice of solvent was also investigated and it was shown that THF facilitated the highest catalyst activity. The only other solvent in which activity was observed was ethyl acetate, where 14% of hydrogenation product **98** was observed (see Experimental, Section 6.5.4, p. 131).

As the reaction concentration appeared to influence the outcome of the reaction, two experiments were carried out using an excess of organosilane (Scheme 61). In an excess of phenylsilane, the hydrogenation and hydrosilylation products, **98** and **99**, were observed in the crude reaction mixture as a 50:50 mixture. Although this results in a slight increase in the yield of hydrosilylation product **99**, the reaction is still unselective for hydrogenation or hydrosilylation. When triethoxysilane was used in excess, the result was the same as all previous reactions giving only hydrogenation product **98**, suggesting that only one reactive intermediate is being formed and so triethoxysilane could be used as a reagent for a selective hydrogenation of vinyl arenes catalysed by titanium. The remaining starting material from this reaction could have been consumed in some other part of the reaction process, such as oligomerisation, which may explain the unchanging yield when an increased amount of triethoxysilane was used. In order to confirm this, a sample of crude reaction mixture should be submitted to GC-MS analysis to see whether any high molecular weight products are observed.

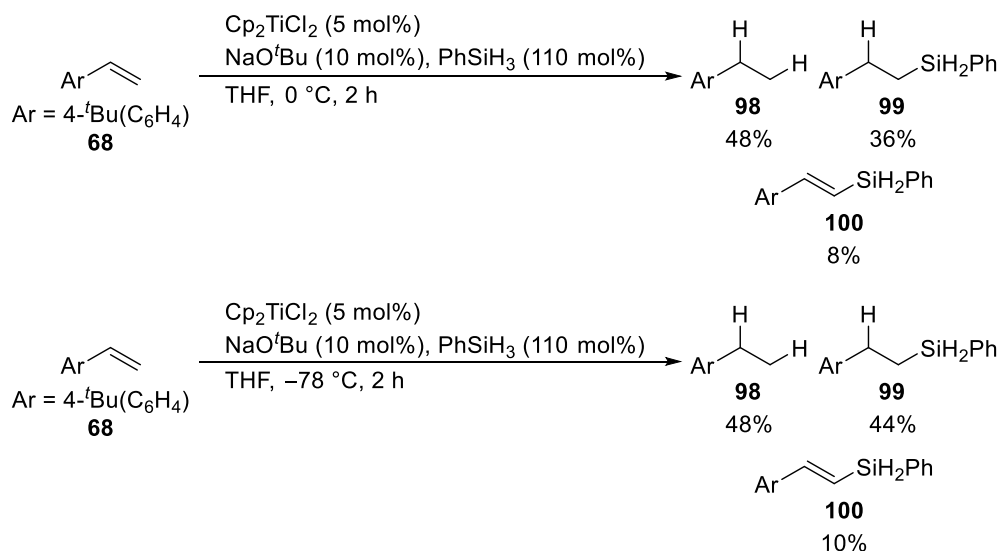


**Scheme 61:** Carrying out reactions in an excess of organosilane.

Two other commercially available titanium catalysts were also investigated alongside titanocene dichloride, titanium tetrachloride and titanium(IV) isopropoxide. Unfortunately, neither pre-catalyst showed any promising activity, although in the case of TiCl<sub>4</sub> there was a significant loss of starting material, presumed to be due to polymerisation. The loading of titanium pre-catalyst, Cp<sub>2</sub>TiCl<sub>2</sub>, was then investigated; halving the loading of both pre-catalyst and alkoxide activator caused no reaction to take place. When the pre-catalyst and sodium *tert*-butoxide activator loadings were doubled, however, the reaction proceeded to give hydrogenation and hydrosilylation products, **98** and **99**, both in 45% yield (90% yield total). These results in combination with previous results on reaction concentrations and loading of organosilane all indicate that a careful balancing of stoichiometry is required.

All reactions thus far were carried out at room temperature, and, after noting the reactions were exothermic,

reactions at lower temperatures were also investigated. At both 0 °C and –78 °C, the reactions proceeded in a similar manner to the previous reactions carried out (Scheme 62).



**Scheme 62:** Titanium-catalysed hydrosilylation reactions at 0 °C and –78 °C.

As none of the above experiments had affected the product distribution significantly, several additives were used in conjunction with the pre-catalyst (Table 13). Considering the product of a hydrogenation reaction was present in all cases, norbornadiene **127** and norbornene **128** were added to reactions as they are both known to be hydrogen acceptors.<sup>98</sup> With norbornadiene **127**, hydrogenation product **98** was the major product (50% yield), with hydrosilylation and dehydrogenative silylation products, **99** and **100**, also being observed in low yields (17% and 9% respectively) (Table 13, Entry 1). This counterintuitive result seems to suggest that the presence of norbornadiene favours the hydrogenation product of styrene, although it was unclear what products (if any) were formed by reaction with norbornadiene. Upon using norbornene **128** as an additive, however, the product distribution of the reaction is similar to that of a reaction in the absence of any additive (Table 13, Entry 2). This suggests that the strained bond in norbornene may have no interaction with the titanium catalyst. Other ligands/additives were also screened to determine whether they might have any stabilising effect on reaction intermediates. The addition of triphenylphosphine **129** as a ligand appeared to have little effect, although the yield of dehydrogenative silylation product **100** was slightly increased in relation to the hydrosilylation product **99** (Table 13, Entry 3). Acetonitrile **130** shut down reactivity entirely, most likely through competitive binding to the titanium catalyst (Table 13, Entry 4). The inclusion of a bidentate ligand such as TMEDA **131** in the reaction mixture appeared to have little effect on product distribution although again the yield of dehydrogenative silylation product **100** was slightly increased in relation to the yield of hydrosilylation product **99** (Table 13, Entry 5). In order to

determine whether the reaction was proceeding through a one-electron mechanism, a radical inhibitor, TEMPO **132**, was added (Table 13, Entries 6 and 7). At loadings of both 100 mol% and 10 mol% no reaction took place, however the lower loading of TEMPO **132** inhibiting the reaction suggests that this may be due to coordination to the catalyst rather than reaction with any radicals being formed. An alternative hydrogen acceptor, acetophenone **133**, was also screened as it was hypothesised that the polarised C=O bond might more readily accept hydrogen. As with many of the previous reactions, however, the product distribution was largely unaffected (Table 13, Entry 8). The product of acetophenone reduction, 1-phenylethanol, was observed in low yields (~20%) in the <sup>1</sup>H NMR spectrum, however it appears as though the titanium-catalysed process shows mostly good chemoselectivity for carbon-carbon double bonds.

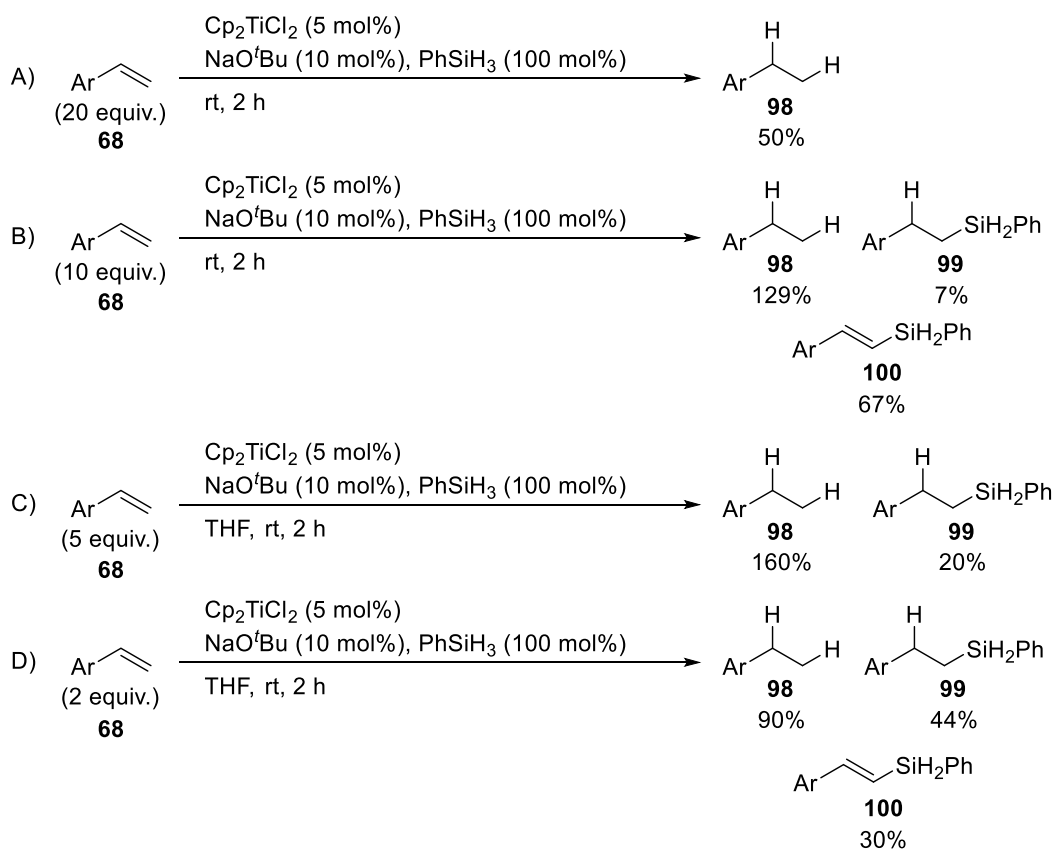
**Table 13:** Effect of additives on the titanium-catalysed hydrogenation/hydrosilylation.

$  \begin{array}{c}  \text{Cp}_2\text{TiCl}_2 \text{ (5 mol\% ), NaO}^t\text{Bu (10 mol\% )} \\  \text{Additive (x mol\% )} \\  \text{PhSiH}_3 \text{ (110 mol\% )} \\  \text{THF, rt, 1 h}  \end{array}  \longrightarrow  \begin{array}{cc}  \begin{array}{c} \text{H} \\   \\ \text{Ar}-\text{CH}-\text{CH}_2-\text{H} \end{array} & \begin{array}{c} \text{H} \\   \\ \text{Ar}-\text{CH}-\text{CH}_2-\text{SiH}_2\text{Ph} \end{array} \\  \mathbf{98} & \mathbf{99} \\  & \begin{array}{c} \text{Ar}-\text{CH}=\text{CH}-\text{SiH}_2\text{Ph} \\ \mathbf{100} \end{array}  \end{array}  $				
Entry	Additive (x mol%)	98 (%) <sup>a</sup>	99 (%) <sup>a</sup>	100 (%) <sup>a</sup>
1 <sup>b</sup>	 (100) <b>127</b>	50	17	9
2 <sup>b</sup>	 (200) <b>128</b>	45	42	10
3 <sup>c</sup>	PPh <sub>3</sub> (10) <b>129</b>	41	34	20
4 <sup>c</sup>	MeCN (10) <b>130</b>	-	-	-
5	 (10) <b>131</b>	47	27	23
6	 (100) <b>132</b>	-	-	-
7	 (10) <b>132</b>	-	-	-
8	 (100) <b>133</b>	50	20	21

<sup>a</sup>Yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.<sup>b</sup>Phenylsilane (210 mol%) was used. <sup>c</sup>Phenylsilane (120 mol%) was used.

As the concentrations of other reagents had been screened, the reaction was then investigated using large excesses of 4-*tert*-butylstyrene **68**. Initially, 20 equivalents of the styrene derivative with respect to phenylsilane was used. (Scheme 63, A). Under these conditions, hydrogenation product **98** was the sole

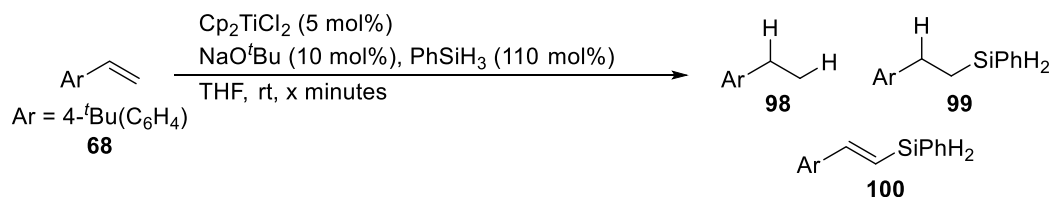
product in a 50% yield (with respect to phenylsilane). The large excess of alkene in this case may be suppressing the catalytic activity by coordination to the titanium. Thus, a slightly lower excess of styrene derivative **67** was then used. Carrying out the reaction with 10 equivalents of 4-*tert*-butylstyrene **68** resulted in the hydrogenation, hydrosilylation and dehydrogenative silylation products, **98**, **99** and **100**, all being formed (Scheme 63 B). Significantly, hydrogenation product **98** was observed in a 129% yield, indicating that one equivalent of phenylsilane can provide more than one atom of hydrogen. Hydrogen generation could result from two reaction pathways: dehydrogenative silylation of the alkene and silane oligomerisation.<sup>92b</sup> This might suggest that unless detrimental side reactions such as silane oligomerisation can be controlled, the formation of hydrogenation products in these reactions are inevitable. Dehydrogenative silylation product **100** was observed in a significantly higher yield than seen previously (67%) and hydrosilylation product **99** was only observed in a 7% yield. Using 5 equivalents of styrene derivative **68** resulted in the formation of hydrogenation product **98** in a 160% yield (with respect to phenylsilane) and hydrosilylation product **99** in 20% yield (Scheme 63, C). With just two equivalents of styrene derivative **68**, hydrogenation product **98** was observed in 90% yield, hydrosilylation product **99** in 44% yield and dehydrogenative silylation product **100** in 30% yield (Scheme 63, D).



**Scheme 63:** Reactions using large excesses of styrene derivative.

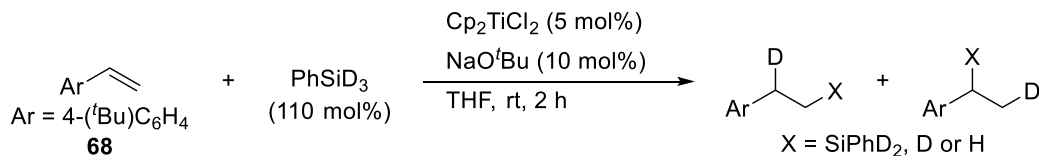
In order to determine how fast the reaction was taking place, and to see whether it was possible to determine which products were forming first, the reaction was monitored by taking aliquots and analysing by  $^1\text{H}$  NMR spectroscopy at regular time intervals (Table 14). From these results, it appeared that hydrogenation product **98** was the first to form, followed by hydrosilylation product **99** and then dehydrogenative silylation product **100**. The formation of hydrogenation product **98** appeared to occur rapidly over the course of the first ten minutes and then plateauing off, peaking at a 32% yield after 1 hour. After an initial period, dehydrogenative silylation product **100** formed rapidly, reaching a maximum yield of 13% after approximately 5 minutes (measurements not completely accurate, due to human error in acquiring aliquots). Hydrosilylation product **99** formed the slowest, although it can be observed forming before the dehydrogenative silylation product **100**. The rate of formation does appear to increase over time, possibly due to a reduction of dehydrogenative silylation product **100** taking place once a certain concentration of this product is reached. The yield of **99** continued to increase over time with the final yield being approximately 32% after 1 hour.

**Table 14:** Monitoring the reaction time of titanium-catalysed reduction of 4-*tert*-butylstyrene.

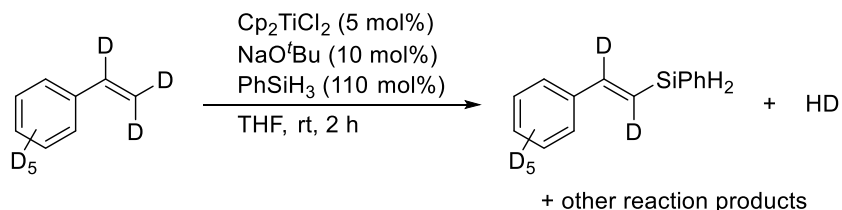


Time (min)	98 (%)	99 (%)	100 (%)	Time (min)	98 (%)	99 (%)	100 (%)
0.5	1.5	-	-	3	9	2.5	5
1	1.5	-	-	5	15	5	12
1.5	3	0.5	-	10	19	10	15
2	5	1	2	30	22	17	12
2.5	6	2	4	60	32	31.5	13

Analysis of the  $^1\text{H}$  and  $^2\text{D}$  NMR spectra following a reaction using  $\text{d}_3$ -phenylsilane showed incorporation of deuterium at the benzylic and homo-benzylic positions, which was expected, and confirmed that the hydrometallation of the carbon-carbon double bond is highly reversible (Scheme 64). Analysis of the  $^1\text{H}$  NMR spectrum after a reaction with  $\text{d}_8$ -styrene revealed a 1:1:1 triplet at 4.47 ppm. This is assumed to be the formation of HD *in situ*, presumably produced from the formation of dehydrogenative silylation product **100** (Scheme 65).

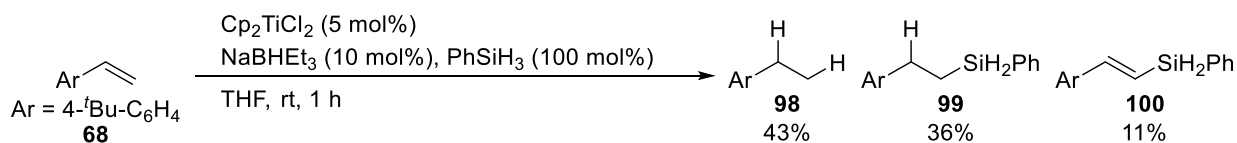


**Scheme 64:** Hydrosilylation reaction using d<sub>3</sub>-phenylsilane.



**Scheme 65:** Formation of HD through a Ti-catalysed dehydrogenative silylation of d<sub>8</sub>-styrene.

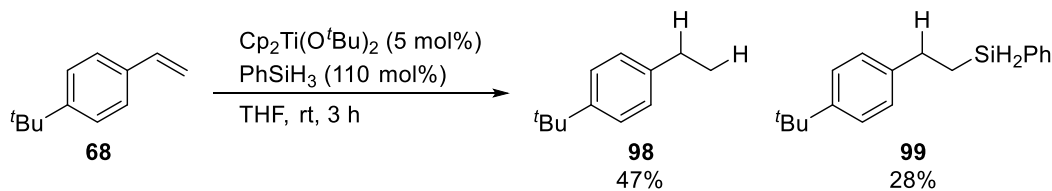
It was important to compare the reaction activated by an alkoxide salt with that of a reaction with a more traditional hydride source. Thus, a reaction was carried out using sodium triethylborohydride in place of sodium *tert*-butoxide (Scheme 66). As with the sodium *tert*-butoxide activated reactions, there was a distribution of three products giving moderate yields of hydrogenation product **98** and hydrosilylation product **99** with a lower yield of dehydrogenative silylation product **100**.



**Scheme 66:** Titanium-catalysed reduction of 4-*tert*-butylstyrene using NaBHET<sub>3</sub> as an activator.

It is also possible that a salt metathesis between titanocene dichloride and sodium *tert*-butoxide takes place under reaction conditions to give a *tert*-butoxide titanium complex. This could then undergo a  $\sigma$ -bond metathesis type reaction with phenylsilane to yield a titanium hydride complex, as an alternative to a hydride transfer from a hypervalent species. Therefore, the titanocene di-*tert*-butoxide complex was synthesised and used in a reaction with styrene derivative and phenylsilane (Scheme 67). No dehydrogenative silylation product **100** was observed, however hydrogenation and hydrosilylation products, **98** and **99**, were observed in similar yields to those obtained earlier. These results suggest that a salt metathesis may take place under the current reaction conditions, although it could be coincidental that this reaction gives a similar result to that of the titanocene dichloride reaction activated with sodium *tert*-butoxide as both presumably proceed through a titanium hydride complex.

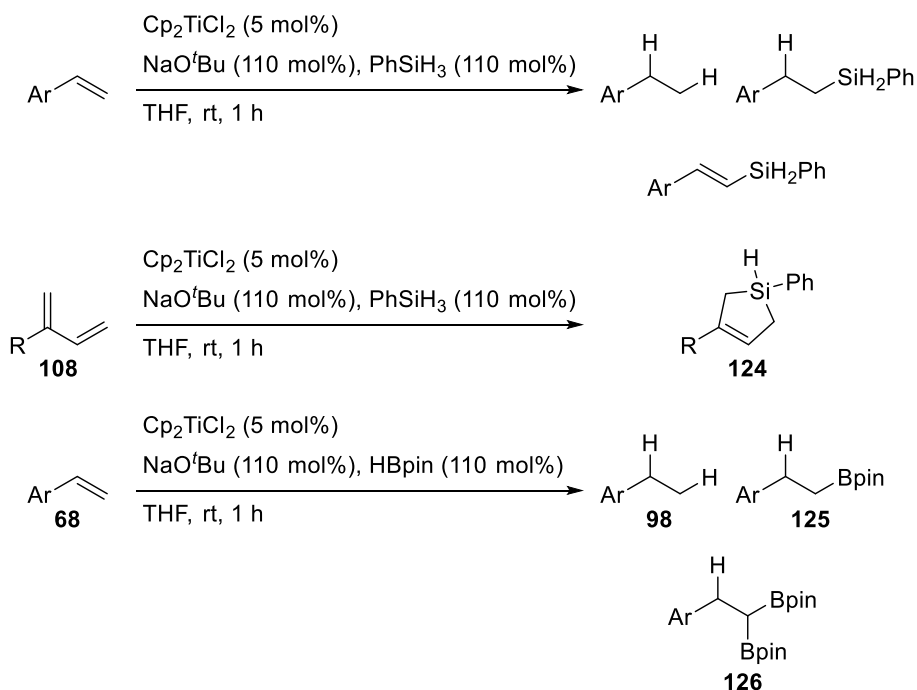




**Scheme 67:** Reaction using titanocene di-*tert*-butoxide complex.

### 4.3: Conclusions and Future Work

Using a new activation method developed in the Thomas group, a titanium-catalysed reduction of olefins was investigated (Scheme 68). In reactions with phenylsilane, a distribution of hydrogenation, hydrosilylation and dehydrogenative silylation was observed with several different olefins, although styrene derivatives gave the best results. The reaction with myrcene **109** gave a cyclic dehydrogenative silylation product **124** as the sole product in moderate yield. Reactions of styrene derivatives with triethoxysilane gave only the hydrogenation product whereas other organosilanes were unreactive. A hydroboration of 4-*tert*-butylstyrene **68** under the same reaction conditions also gave a moderate yield of the hydroboration product **125** and a low yield of what was presumed to be the 1,1-diboration product **126**.



**Scheme 68:** The attempted titanium-catalysed hydrosilylation and hydroboration reactions carried out and the products observed.

Carrying out reactions at different concentrations and with excesses of different reagents did not significantly alter the product distribution although using an excess of styrene revealed that multiple

hydrogen additions could occur from one equivalent of phenylsilane, and in some cases dehydrogenative silylation was favoured. The addition of different additives and ligands also had little effect on product distribution.

Monitoring a reaction by  $^1\text{H}$  NMR revealed that hydrogenation product **98** was the first and fastest to form in the titanium-catalysed reaction. Hydrosilylation product **99** was formed slowly at first, after what appeared to be an initial induction period. The formation of dehydrogenative silylation product **100** stopped after approximately 5 minutes. The reaction with a more traditional hydride source also gave the same distribution of products suggesting that the reaction proceeded through a similar mechanism, although a  $\sigma$ -bond metathesis type activation using a titanocene di-*tert*-butoxide complex also gave similar results.

Future work using the system reported above should focus on the cyclic dehydrogenative silylation of 1,3-dienes although a degree of novelty would be required to separate it from the work reported by Möise *et al.*<sup>96</sup> To improve selectivity and reactivity with other alkenes, more well-defined titanium complexes using a variety of ligand frameworks could be investigated. Perhaps if the reaction could be better controlled through the design of a titanium complex, then the process could be better understood, and that knowledge carried forward to a simpler system using commercially available starting materials.

## Chapter 5: Conclusions

With regards to the original aims, the initial goal of further developing a general iron-catalysed hydrofunctionalisation using a single set of reaction conditions was met. The methodology used commercially-available starting materials, under mild conditions, to furnish a range of products in moderate to excellent yields. In previous work, the reaction mechanism had proposed to proceed through a benzylic Grignard reagent which was then capable of reacting with an electrophile, and in the work discussed a range of electrophiles were shown to be compatible. Unfortunately, development of the methodology beyond styrene derivatives had limited success, with aromatic diene substrates undergoing a formal hydrosilylation in only moderate yields despite various changes to reaction conditions.

The secondary aim of this research was to develop novel reactivity with other Earth-abundant metals, including magnesium and titanium. Previous work in the literature had demonstrated the capability for well-defined magnesium complexes to act as catalysts in the hydroboration of carbonyls and imines. The attempt to expand upon this work was unsuccessful, although the hydroboration product of an alkyne substrate was observed in 9% yield. Since this product could possibly form from the reaction with trace amounts of  $\text{BH}_3$  and there was no potential to move away from the highly air- and moisture-sensitive catalysts, the reaction was not pursued.

The research into a titanium-catalysed hydrofunctionalisation of alkenes was more successful. The use of commercially available  $\text{Cp}_2\text{TiCl}_2$  in conjunction with an alkoxide activator led to an active catalyst that was demonstrated to react with styrene derivatives and a 1,3-diene, myrcene. The work looked mostly into the hydrosilylation reaction using phenylsilane as the reductant, giving a mixture of the hydrogenation, hydrosilylation and dehydrogenative silylation in most cases. The hydroboration of a styrene derivative was also briefly examined. While a selective reaction was not found, the groundwork was laid for further work into the use of titanium as a catalyst for hydrofunctionalisation of alkenes.

## Chapter 6: Experimental

### 6.1: General Experimental

All air and moisture sensitive reactions were carried out either using standard vacuum line and Schlenk techniques, or in a glovebox with a purified nitrogen atmosphere. All solvents for air- and moisture sensitive techniques were obtained from an anhydrous solvent system (Innovative Technology). All glassware was cleaned using base (KOH, *i*-PrOH) and acid (HCl<sub>(aq)</sub>) baths.

Iron(II) chloride tetrahydrate was purchased from Sigma Aldrich (UK); puriss. p.a., >99.0% (product number 44939. Lot BCBF5170V). Iron(II) chloride was purchased from Strem Chemicals Inc. (UK); anhydrous iron chloride, 98% (product number 93-2631. Lot 19226800, 44.00000% Fe, expect 44.059%). *N,N,N',N'*-Tetramethylethylenediamine (TMEDA), 2,2'-bipyridyl and 1,10-phenanthroline were purchased from Sigma Aldrich (UK). 2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine was prepared according to a literature procedure.<sup>99</sup> All styrene derivatives and electrophiles used were purchased from Sigma Aldrich, Alfa Aesar, Acros Organics and Apollo Scientific, UK, or synthesised within the laboratory. Ethylmagnesium bromide, *n*-butyllithium and dibutylmagnesium were purchased from Sigma Aldrich (UK). All reagents were used as received.

All <sup>1</sup>H, <sup>13</sup>C, <sup>11</sup>B and <sup>19</sup>F spectra were obtained on Bruker Avance III 400 and 500 MHz spectrometers or on a Bruker Avance I 600 MHz spectrometer. All spectra were obtained at ambient temperature. The chemical shifts ( $\delta$ ) and coupling constants (*J*) were recorded in parts per million (ppm) and Hertz (Hz) respectively. <sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F multiplicities and coupling constants are reported where applicable. Coupling constants (*J*) are quoted to the nearest 0.5 Hz. Spectra were recorded relative to the residual solvent residual peak (CDCl<sub>3</sub> at 7.27 ppm and 77.00 ppm).

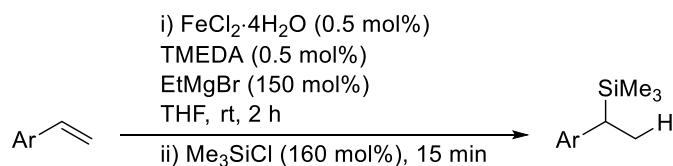
Aqueous sulphate buffer was prepared by dissolving Na<sub>2</sub>SO<sub>4</sub> (1.5 mol) and H<sub>2</sub>SO<sub>4</sub> (0.5 mol) in water and adding water to give a total volume of 2000 mL. Flash chromatography was performed on silica gel (Merck Kieselgel 60). Analytical thin layer chromatography was performed on aluminium backed silica plates (60 F<sub>254</sub>). Pet. ether refers to petroleum ether 40-60.

Infra-red spectra were recorded on a Shimadzu IRAffinity-1 spectrometer (serial no. A213749). Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. High resolution mass spectra were recorded on a Thermo/Finnigan MAT 900 mass spectrometer.

## 6.2: Iron-catalysed Hydrofunctionalisation of Vinylarenes

### 6.2.1: General Procedures

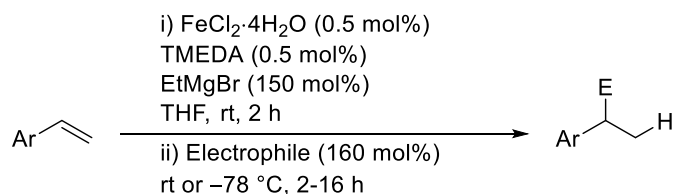
#### General Procedure A: Hydrosilylation of styrene derivatives



*N,N,N',N'*-Tetramethylethylenediamine (TMEDA) (5  $\mu$ L, 0.035 mmol) was added to a stirred solution of FeCl<sub>2</sub>·4H<sub>2</sub>O (7 mg, 0.035 mmol) in anhydrous THF (5 mL) under nitrogen and stirred for 5 min. 0.5 mL of this solution was transferred to a flask containing 4.5 mL anhydrous tetrahydrofuran under nitrogen. A styrene derivative (0.7 mmol) was added to the flask and ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.35 mL, 1.1 mmol) was added dropwise. The reaction was stirred for 2 h and trimethylsilyl chloride (0.14 mL, 1.1 mmol) added. The reaction was stirred for a further 15 min and quenched with aqueous sulphate buffer solution (10 mL). The phases were separated and the aqueous phase extracted with Et<sub>2</sub>O (3 x 10 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (MgSO<sub>4</sub>) and trimethoxybenzene (23.5 mg, 0.14 mmol) added as an internal standard. The solvent was removed *in vacuo* and the yield for the reaction determined by <sup>1</sup>H NMR spectroscopy.

Known products were identified by <sup>1</sup>H NMR spectroscopy and characterised by comparison with authentic samples of spectral data.

#### General Procedure B: Hydrofunctionalisation of styrene derivatives

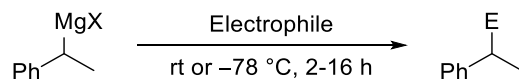


*N,N,N',N'*-Tetramethylethylenediamine (TMEDA) (5  $\mu$ L, 0.035 mmol) was added to a stirred solution of FeCl<sub>2</sub>·4H<sub>2</sub>O (7 mg, 0.035 mmol) in anhydrous THF (5 mL) under nitrogen and stirred for 5 mins. 0.5 mL of this solution was transferred to a flask containing 4.5 mL anhydrous THF under nitrogen. Styrene (0.7 mmol) was added to the flask and ethylmagnesium halide (1.5 mmol) was added dropwise. The reaction was stirred for 2 h and the electrophile (1.6 mmol) added, either neat or as a solution in anhydrous THF (1 M), at room temperature or at -78 °C. The reaction was stirred for a further 2 h and quenched with aqueous sulphate buffer solution or water (10 mL). The phases were separated and the aqueous phase extracted with

Et<sub>2</sub>O (3 x 10 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*.

Known products were identified by <sup>1</sup>H NMR spectroscopy and characterised by comparison with authentic samples of spectral data.

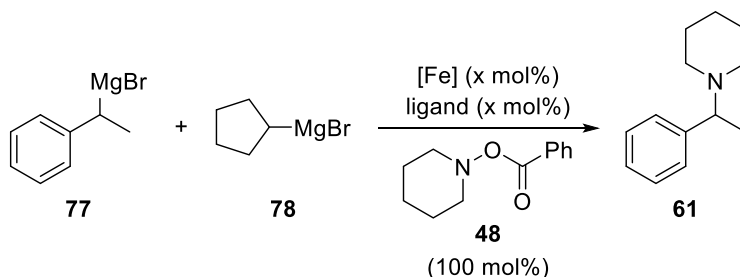
### General Procedure C: Reaction with benzylic Grignard reagent



Electrophile (1.6 equiv.) was added either neat or as a solution in anhydrous THF (2 mL) to 1-phenylethyl magnesium chloride (0.7 mmol) in anhydrous THF (5 mL). Solution was stirred at room temperature or -78 °C for 2 - 16 h and then quenched with aqueous sulphate buffer solution (10 mL). The phases were separated and the aqueous phase extracted with Et<sub>2</sub>O (3 x 10 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*.

Products were identified by <sup>1</sup>H NMR spectroscopy and yields calculated against 20 mol% 1,3,5-trimethoxybenzene as internal standard.

### General Procedure D: Investigating the reactivity of the benzylic Grignard reagent

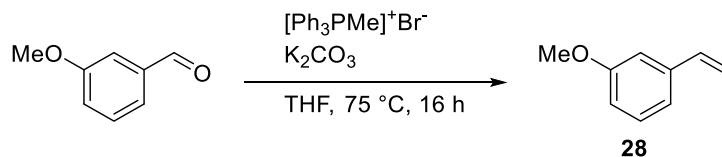


To a solution of (1-phenylethyl)magnesium bromide **77**, cyclopentylmagnesium bromide **78**, iron salt [Fe], and ligand in THF, a solution of *O*-benzoyl-*N*-hydroxypiperidine **48** in THF was added dropwise over 1 h at 0 °C. The reaction mixture was left to stir for a further 1 h and quenched with sat. aq. NaHCO<sub>3</sub>. The aqueous phase was then extracted with Et<sub>2</sub>O (3 x 10 mL) and the combined organic phases washed with water (10 mL), brine (10 mL), dried over Mg<sub>2</sub>SO<sub>4</sub> and dried *in vacuo*. The yield was then determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-methoxybenzene as an internal standard.

## 6.2.2: Synthesis of Reagents

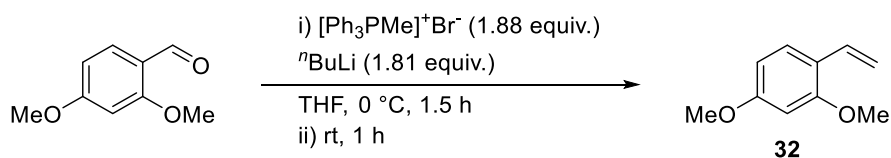
### Synthesis of Styrene Derivatives

#### 3-Methoxy-1-vinylbenzene (**28**)



*m*-Anisaldehyde (4.48 mL, 36.7 mmol), methyltriphenylphosphonium bromide (15.7 g, 44.0 mmol) and potassium carbonate (8.12 g, 58.8 mmol) were added together in anhydrous THF (50 mL) under nitrogen. The reaction was heated to reflux for 16 hours, then cooled to room temperature, filtered and the solvent removed *in vacuo*. The residue was dissolved in hot pentane (50 mL), cooled to 0 °C to precipitate triphenylphosphine oxide, filtered and washed with cold pentane (20 mL). The filtrate was concentrated *in vacuo* and passed through a short plug of silica gel (pet. ether/Et<sub>2</sub>O 9:1) to give 3-methoxy-1-vinylbenzene **28** (4.69 g, 95%) as a colourless oil. *R*<sub>f</sub> 0.76 (pet. ether/EtOAc 9:1); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.29-7.24 (1H, m, ArH), 7.06-7.01 (1H, m, ArH), 7.00-6.96 (1H, m, ArH), 6.87-6.82 (1H m, ArH), 6.72 (1H, dd, *J* = 17.5, 11.0 Hz, CH=CH<sub>2</sub>), 5.77 (1H, d, *J* = 17.5 Hz, CH=CH<sub>a</sub>H<sub>b</sub>), 5.28 (1H, d, *J* = 11.0 Hz, CH=CH<sub>a</sub>H<sub>b</sub>), 3.85 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 159.8 (C), 139.0 (C), 136.8 (CH), 129.5 (CH), 118.9 (CH), 114.1 (CH<sub>2</sub>), 113.4 (C), 111.5 (CH), 55.2 (CH<sub>3</sub>). Data consistent with literature.<sup>57</sup>

#### 2,4-Dimethoxy-1-vinylbenzene (**32**)

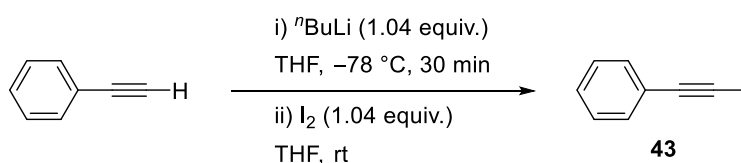


To an ice-cold mixture of methyltriphenylphosphonium bromide (12.2 g, 34 mmol) in anhydrous THF (56 mL), *n*-butyllithium (1.6 M in hexanes, 20.4 mL, 32.7 mmol) was added dropwise and stirred at 0 °C for 1.5 hours. A solution of 2,4-di(methoxy)-benzaldehyde (3 g, 18 mmol) in anhydrous THF (56 mL) was then added, the mixture brought to room temperature and stirred for a further 1 hour. The mixture was diluted with sat. aq. NH<sub>4</sub>Cl (50 mL), the phases separated and the organic phase extracted with Et<sub>2</sub>O (2 × 20 mL). The combined extracts were washed with sat. aq. NaCl and dried (MgSO<sub>4</sub>). The solvent was removed *in vacuo* and passed through a short plug of silica gel (pet. ether/EtOAc 9:1) to give 2,4-dimethoxy-1-vinylbenzene **32** (1.45 g, 49%) as a colourless oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.42 (1H, d,

$J = 8.5$  Hz, ArH), 7.02 – 6.94 (1H, m, CH=CH<sub>2</sub>), 6.54 – 6.49 (1 H, m, ArH), 6.47 (1 H, d,  $J = 2.40$  Hz, ArH), 5.65 (1 H, dd,  $J = 17.7, 1.6$  Hz, CH=CH<sub>a</sub>H<sub>b</sub>), 5.17 (1H, dd,  $J = 11.2, 1.6$  Hz, CH=CH<sub>a</sub>CH<sub>b</sub>), 3.86 (3H, s, OCH<sub>3</sub>), 3.84 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  160.7 (C), 158.0 (C), 131.4 (CH), 127.4 (CH), 120.1 (C), 112.4 (CH), 104.9 (CH), 98.5 (CH<sub>2</sub>), 55.6 (CH<sub>3</sub>), 55.5 (CH<sub>3</sub>). Data consistent with literature values.<sup>100</sup>

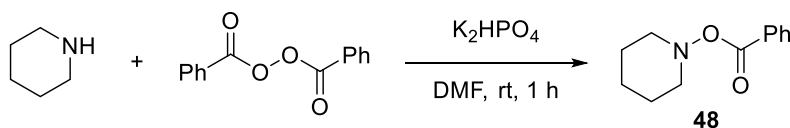
## Synthesis of Electrophiles

### 1-Iodophenylacetylene (43)



Phenylacetylene (2.2 mL, 20 mmol) was added to anhydrous THF (18 mL) and the mixture was cooled to  $-78\text{ }^\circ\text{C}$ . *n*-Butyllithium (1.6 M in hexanes, 13 mL, 20.8 mmol) was added dropwise and the reaction mixture was stirred at  $-78\text{ }^\circ\text{C}$  for 30 minutes. A solution of iodine (5.3 g, 20.8 mmol) in anhydrous THF (19 mL) was added slowly *via* cannula and the solution slowly warmed to room temperature. The mixture was then diluted with water (50 mL), the phases separated and the organic phase extracted with pentane (3 x 20 mL). The combined extracts were washed with sat. aq. Na<sub>2</sub>SO<sub>3</sub> and sat. aq. NaCl. The solvent was removed *in vacuo* and passed through a short plug of silica gel (pentane) to give 1-iodophenylacetylene **43** (4.25 g, 93%) as a yellow oil. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.46-7.44 (2H, m, ArH), 7.34-7.30 (3H, m, ArH); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  132.3 (2 x CH), 128.9 (CH), 128.3 (2 x CH), 123.5 (C), 94.2 (C), 6.2 (C). Data consistent with literature.<sup>101</sup>

### *O*-Benzoyl-*N*-hydroxypiperidine (48)



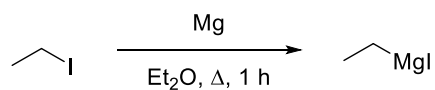
To a suspension of benzoyl peroxide (3.03 g, 12.5 mmol) and K<sub>2</sub>HPO<sub>4</sub> (2.09 g, 12 mmol) in DMF (32 mL), piperidine (1.5 mL, 15 mmol) was added in one portion. The reaction was then stirred for 1 hour at room temperature. The mixture was then diluted with water until all solids had dissolved and the organic phase extracted with EtOAc (3 x 10 mL) and washed with saturated NaHCO<sub>3</sub> solution (2 x 10 mL). The combined aqueous fractions were then washed with EtOAc (3 x 10 mL). All organic fractions were then combined and washed with water (3 x 10 mL), brine (100 mL), dried over MgSO<sub>4</sub> and then concentrated *in vacuo*.



The resulting crude product was purified by flash chromatography (pet. ether/EtOAc 3:1) to give **48** as a white crystalline solid (1.44 g, 47%).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (2H, app. d, ArH), 7.56 (1H, app. t, ArH), 7.44 (2H, app. t, ArH), 3.52 (2H, br. s), 2.79 (2H, br. s), 1.89-1.80 (4H, m), 1.69 (1H, br. s), 1.31 (1H, br. s);  $^{13}\text{C}$  NMR (125.8 MHz,  $\text{CDCl}_3$ )  $\delta$  164.9 (C), 133.0 (C), 129.9 (CH), 129.6 (2  $\times$  CH), 128.5 (2  $\times$  CH), 57.7 (2  $\times$   $\text{CH}_2$ ), 25.1 (2  $\times$   $\text{CH}_2$ ), 23.5 ( $\text{CH}_2$ ). Data consistent with literature.<sup>102</sup>

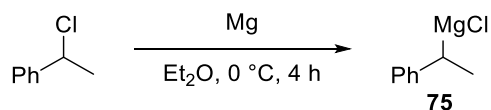
## Synthesis of Grignard Reagents

### Ethylmagnesium iodide



In an oven-dried flask under an inert atmosphere, magnesium turnings (243 mg, 10 mmol) were suspended in  $\text{Et}_2\text{O}$  (20 mL) and heated to approx. 30 °C with very occasional stirring. To this iodoethane (0.08 mL, 1 mmol) was added dropwise in order to initiate the reaction. Upon initiation, the remaining iodoethane (0.72 mL, 9 mmol) was added and the reaction heated at reflux for 1 h. The solution was allowed to settle and then transferred by syringe to a clean, oven-dried Schlenk flask equipped with a Young's tap. The concentration was determined to be 0.19 M by titration against 2-hydroxybenzaldehyde phenylhydrazone (26.5 mg, 0.125 mmol).

### 1-Phenylethylmagnesium chloride (**75**)

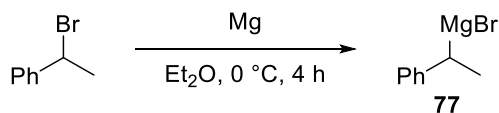


Prepared according to a procedure reported by Brown.<sup>68</sup>

Magnesium turnings (3.20 g, 132 mmol) were added to an oven-dried Schlenk tube with a magnetic stirrer bar and sealed with a pressure-equalising dropping funnel. The vessel was back-filled 3 times with nitrogen and the magnesium turnings were stirred vigorously overnight under a nitrogen atmosphere. After stirring overnight the magnesium turnings appeared dark grey, and the bottom of the flask and the stirrer bar had a metallic coating. Anhydrous diethyl ether (~10 mL) was added until the turnings were covered. The solution was cooled to 0 °C and to this a solution of 1-chloro-1-phenylethane (2.65 mL, 20 mmol) in anhydrous  $\text{Et}_2\text{O}$  (20 mL) was added over 3 hours. The reaction was stirred for a further 1 hour at 0 °C. The solution was allowed to settle and then transferred by syringe to an oven-dried Schlenk flask equipped with a

Young's tap and diluted up to 50 mL. The concentration was determined to be 0.31 M by titration against 2-hydroxybenzaldehyde phenylhydrazone (26.5 mg, 0.125 mmol).

### 1-Phenylethylmagnesium bromide (77)

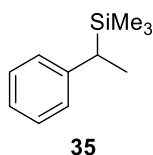


Prepared according to a procedure reported by Brown.<sup>68</sup>

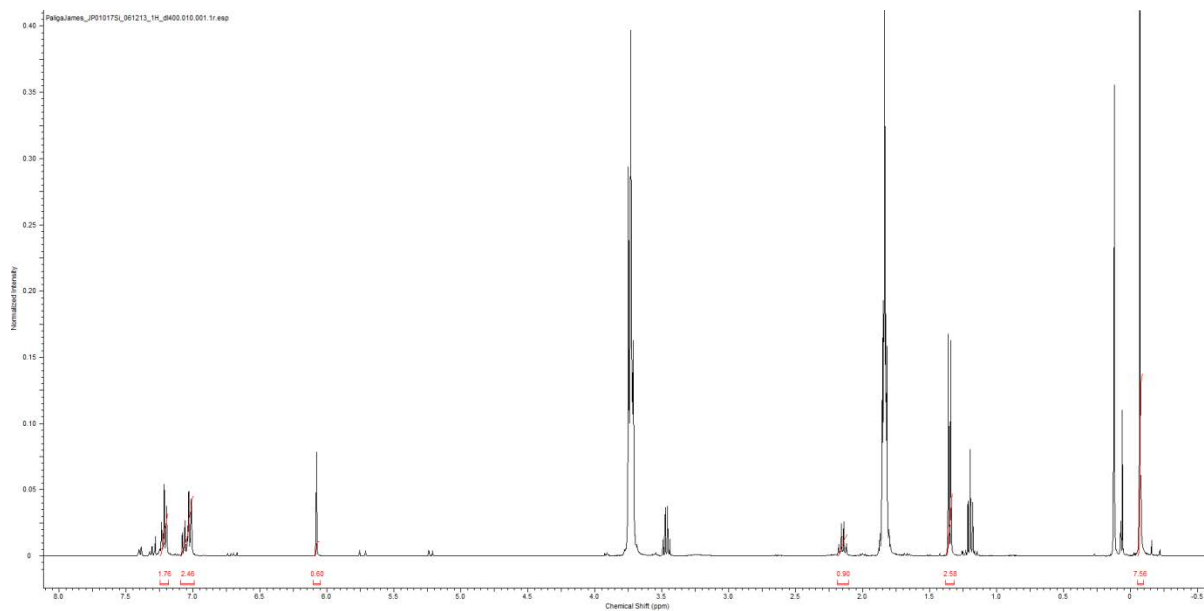
Magnesium turnings (3.20 g, 132 mmol) were added to an oven-dried Schlenk tube with a magnetic stirrer bar and sealed with a pressure-equalising dropping funnel. The vessel was back-filled 3 times with nitrogen and the magnesium turnings were stirred vigorously overnight under a nitrogen atmosphere. After stirring overnight the magnesium turnings appeared dark grey, and the bottom of the flask and the stirrer bar had a metallic coating. Anhydrous diethyl ether (~10 mL) was added until the turnings were covered. The solution was cooled to 0 °C and to this a solution of 1-bromo-1-phenylethane (3.7 mL, 20 mmol) in anhydrous Et<sub>2</sub>O (20 mL) was added over 3 hours. The reaction was stirred for a further 1 hour at 0 °C. The solution was allowed to settle and then transferred by syringe to an oven-dried Schlenck flask equipped with a Young's tap and diluted up to 50 mL. The concentration was determined to be 0.43 M by titration against 2-hydroxybenzaldehyde phenylhydrazone (26.5 mg, 0.125 mmol).

## 6.2.3: Alkene Scope (Table 1, p. 20)

### 1-Phenylethyl-1-trimethylsilane (35)



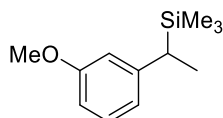
General procedure A was applied to styrene (80  $\mu$ L, 0.7 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (0.7 mg, 0.0035 mmol), TMEDA (0.5  $\mu$ L, 0.0035 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.35 mL, 1.1 mmol) and trimethylsilyl chloride (0.14 mL, 1.1 mmol).



Trimethoxybenzene (20 mol%): 6.08 ppm (3H, s); 1-phenylethyl-1-trimethylsilane **35**: 2.14 ppm (1H, q,  $J$  = 7.6 Hz); 0.9/1 x 100 = 90% yield.

Data was consistent with literature values.<sup>52</sup>

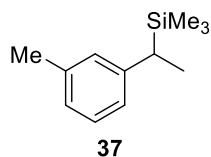
### [1-(3-Methoxyphenyl)ethyl]trimethylsilane (**36**)



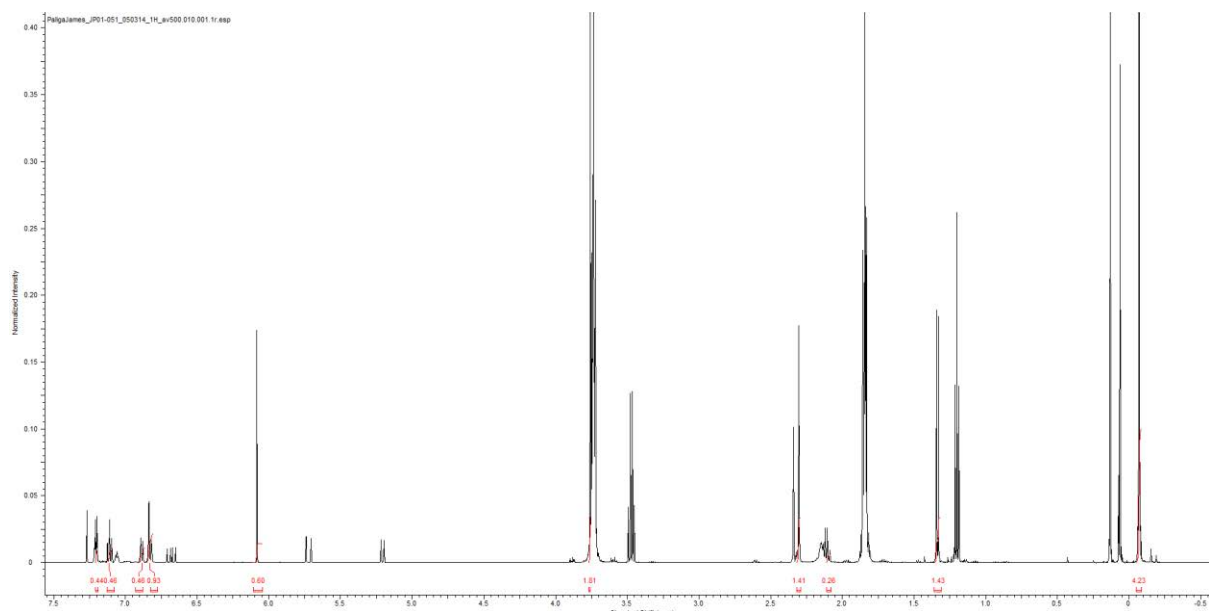
**36**

General procedure A was applied to 3-methoxy-1-vinylbenzene **28** (0.14 mL, 1.0 mmol),  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (1.0 mg, 0.005 mmol), TMEDA (0.7  $\mu\text{L}$ , 0.005 mmol), ethylmagnesium bromide (3 M in  $\text{Et}_2\text{O}$ , 0.50 mL, 1.5 mmol) and trimethylsilyl chloride (0.20 mL, 1.6 mmol). The crude product was purified by flash chromatography (pet. ether  $\rightarrow$  pet. ether/ $\text{Et}_2\text{O}$  97:3) to give [1-(3-methoxyphenyl)ethyl]trimethylsilane **36** as a colourless oil (152 mg, 73%).  $R_f$  0.32 (pet. ether);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.17 (1H, t,  $J$  = 8.0 Hz, ArH), 6.66 (2H, d,  $J$  = 8.0 Hz, ArH), 6.62 (1H, s, ArH), 3.81 (3H, s,  $\text{OCH}_3$ ), 2.17 (1H, q,  $J$  = 7.5 Hz,  $\text{CHCH}_3$ ), 1.37 (3H, d,  $J$  = 7.5 Hz,  $\text{CHCH}_3$ ), -0.03 (9H, s,  $\text{Si}(\text{CH}_3)_3$ );  $^{13}\text{C}$  NMR (125.8 MHz,  $\text{CDCl}_3$ ) 159.4 (C), 147.8 (CH), 128.8 (CH), 119.7 (CH), 113.0 (C), 109.2 (CH), 55.0 ( $\text{CH}_3$ ), 29.9 ( $\text{CH}_3$ ), 14.8 (CH), -3.3 ( $3 \times \text{CH}_3$ ); HRMS (ESI) Exact mass calcd for  $\text{C}_{12}\text{H}_{20}\text{OSiNa}$   $[\text{M}+\text{Na}]^+$ : 231.1176, found: 231.1173.

### [1-(3-Methylphenyl)ethyl]trimethylsilane (**37**)



General procedure A was applied to 3-methyl-1-vinylbenzene (93  $\mu$ L, 0.7 mmol),  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (0.7 mg, 0.0035 mmol), TMEDA (0.5  $\mu$ L, 0.0035 mmol), ethylmagnesium bromide (3 M in  $\text{Et}_2\text{O}$ , 0.35 mL, 1.1 mmol) and trimethylsilyl chloride (0.14 mL, 1.1 mmol).

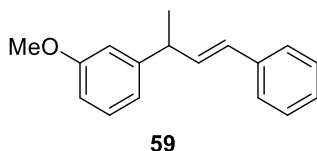


Trimethoxybenzene (20 mol%): 6.08 ppm (3H, s); [1-(3-methylphenyl)ethyl]trimethylsilane **37**: 1.34 ppm (3H, d,  $J = 7.6$  Hz);  $(1.43/3) \times 100 = 48\%$  yield.

Data was compared to similar products in the literature.<sup>52</sup>

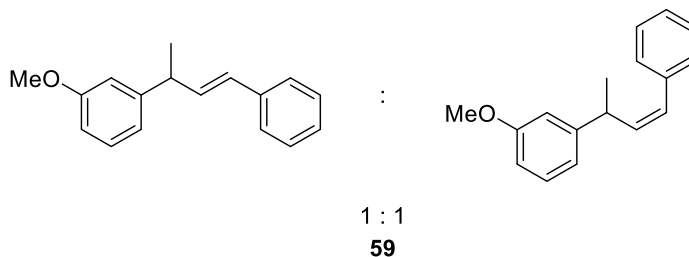
## 6.2.4: Electrophile Scope (Table 2, p. 22)

### 1-Methoxy-3-[(3*E*)-4-phenylbut-3-en-2-yl]benzene (**59**)



General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (0.14 mL, 1 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (1.0 mg, 0.005 mmol), TMEDA (0.7 μL, 0.005 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.5 mL, 1.5 mmol) and β-bromostyrene **44** (0.21 mL, 1.6 mmol). The crude product was purified by flash chromatography (pentane→pentane/Et<sub>2</sub>O 99:1) to give **59** as a yellow oil (187 mg, 78%). R<sub>f</sub> 0.48 (pet. ether/Et<sub>2</sub>O 99:1); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.39-7.35 (2H, m, ArH), 7.30 (2H, t, *J* = 7.5 Hz, ArH), 7.26-7.19 (2H, m, ArH), 6.89 (1H, d, *J* = 7.5 Hz, ArH), 6.86-6.83 (1H, m, ArH), 6.77 (1H, dd, *J* = 8.0, 2.5 Hz, ArH), 6.44 (1H, d, *J* = 16.0 Hz, CHPh), 6.38 (1H, dd, *J* = 16.0, 6.0 Hz, CH=CHPh), 3.82 (3H, s, OCH<sub>3</sub>), 3.63 (1H, quintet, *J* = 7.0 Hz, CHCH<sub>3</sub>), 1.47 (3H, d, *J* = 7.0 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 159.7 (C), 147.4 (CH), 137.6 (CH), 135.0 (CH), 129.4 (C), 128.6 (CH), 128.5 (CH), 127.0 (2 × CH), 126.2 (2 × CH), 119.7 (C), 113.3 (CH), 111.3 (CH), 55.2 (CH<sub>3</sub>), 42.6 (CH), 21.2 (CH<sub>3</sub>). Data consistent with literature values.<sup>103</sup>

### 1-Methoxy-3-(4-phenylbut-3-en-2-yl)benzene (**59**)



General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (97 μL, 0.7 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (0.7 mg, 3.5 × 10<sup>-3</sup> mmol), TMEDA (0.5 μL, 3.5 × 10<sup>-3</sup> mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.35 mL, 1.1 mmol) and α-bromostyrene **45** (0.15 mL, 1.1 mmol). The crude product was purified by flash chromatography (pentane→pentane/Et<sub>2</sub>O 99:1) to give **59** (107 mg, 64%) as a 1:1 inseparable mixture of cis/trans isomers and a colourless oil. R<sub>f</sub> 0.48 (pet. ether/Et<sub>2</sub>O 99:1).

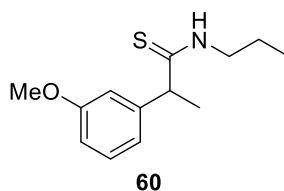
*Cis*-product: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.40-7.18 (6H, m, ArH), 6.90 (1H, d, *J* = 7.5 Hz, ArH), 6.86-6.84 (1H, m, ArH), 6.80-6.75 (1H, m, ArH), 6.51 (1H, d, *J* = 11.5 Hz, CHPh), 5.84 (1H, dd, *J* = 11.5, 10.5 Hz, CH=CHPh), 4.01 (1H, qd, *J* = 10.5, 7.0 Hz, CHCH<sub>3</sub>), 3.82 (3H, s, OCH<sub>3</sub>), 1.41 (3H, d, *J* = 7.0 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 159.8 (C), 147.9 (CH), 137.4 (CH), 136.8 (CH), 129.5 (C),

128.7 (CH), 128.2 (CH), 127.9 (2 × CH), 126.7 (2 × CH), 119.3 (C), 113.0 (CH), 111.1 (CH), 55.1 (CH<sub>3</sub>), 37.8 (CH), 22.9 (CH<sub>3</sub>).

*Trans*-product: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.40-7.18 (6H, m, ArH), 6.90 (1H, d, *J* = 7.5 Hz, ArH), 6.86-6.84 (1H, m, ArH), 6.80-6.75 (1H, m, ArH), 6.44 (1H, d, *J* = 16.0 Hz, CHPh), 6.39 (1H, dd, *J* = 16.0, 6.0 Hz, CH=CHPh), 3.82 (3H, s, OCH<sub>3</sub>), 3.64 (1H, app. quintet, *J* = 7.0 Hz, CHCH<sub>3</sub>), 1.48 (3H, d, *J* = 7.0 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 159.7 (C), 147.4 (CH), 137.6 (CH), 135.0 (CH), 129.4 (C), 128.6 (CH), 128.5 (CH), 127.0 (2 × CH), 126.2 (2 × CH), 119.7 (C), 113.3 (CH), 111.3 (CH), 55.2 (CH<sub>3</sub>), 42.6 (CH), 21.2 (CH<sub>3</sub>).

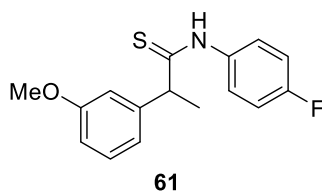
Data were consistent with literature values.<sup>103</sup>

### 2-(3-Methoxyphenyl)-*N*-propylpropane thioamide (**60**)



General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (0.14 mL, 1.0 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (1.0 mg, 0.005 mmol), TMEDA (0.75 μL, 0.005 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.5 mL, 1.5 mmol) and propyl isothiocyanate **46** (0.17 mL, 1.6 mmol). The crude product **60** was obtained as a colourless oil (68% yield by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard). R<sub>f</sub> 0.52 (pet. ether/ethyl acetate 8:2); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.29 (1H, t, *J* = 7.8 Hz, ArH), 7.00 (1H, br. s, NH), 6.91 (1H, d, *J* = 7.7 Hz, ArH), 6.87 (1H, t, *J* = 2.2 Hz, ArH), 6.85 (1H, dd, *J* = 8.2, 2.5 Hz, ArH), 4.08 (1H, q, *J* = 7.2 Hz, BzH), 3.81 (3H, s, OCH<sub>3</sub>), 3.56 (2H, dq, *J* = 6.9, 1.3 Hz, NHCH<sub>2</sub>), 1.70 (3H, d, *J* = 7.2 Hz, ArCHCH<sub>2</sub>), 1.55 (2H, sextet, *J* = 7.3 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 0.84 (3H, t, *J* = 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 207.1 (C), 160.1 (C), 142.4 (CH), 130.1 (CH), 119.9 (C), 113.6 (CH), 113.0 (CH), 55.3 (CH<sub>2</sub>), 55.0 (CH<sub>3</sub>), 47.7 (CH), 21.3 (CH<sub>2</sub>), 21.1 (CH<sub>3</sub>), 11.2 (CH<sub>3</sub>); HRMS (ESI) Exact mass calcd for C<sub>13</sub>H<sub>20</sub>NOS [M+H]<sup>+</sup>: 238.12800, found: 238.12601.

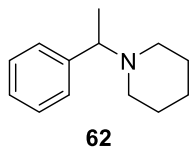
### *N*-(4-Fluorophenyl)-2-(3-methoxyphenyl)propane thioamide (**61**)



General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (97 μL, 0.7 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (0.7

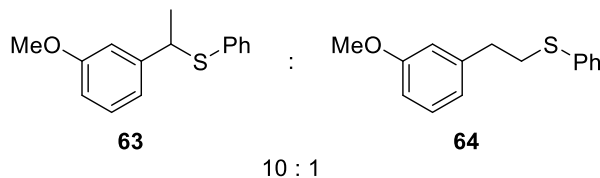
mg, 0.0035 mmol), TMEDA (0.5  $\mu$ L, 0.0035 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.35 mL, 1.1 mmol) and 4-fluorophenyl isothiocyanate **47** (172 mg, 1.12 mmol). The crude product **61** was obtained as a yellow oil (47% yield by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.38 (1H, br. s, NH), 7.47 – 7.42 (2H, m, ArH), 7.33 (1H, t,  $J$  = 7.9 Hz, ArH), 7.05 – 6.94 (4H, m, ArH), 6.87 (1H, ddd,  $J$  = 8.2, 2.6, 0.8 Hz, ArH), 4.19 (1H, q,  $J$  = 7.1 Hz, ArCH), 3.82 (3H, s, OCH<sub>3</sub>), 1.77 (3H, d,  $J$  = 7.2 Hz, ArCHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  207.37 (C), 161.94 (C), 160.44 (C), 159.98 (C), 142.51 (C), 134.79 (d,  $J$  = 3.1 Hz, C), 130.49 (C), 126.11 (d,  $J$  = 8.4 Hz, C), 120.02 (C), 115.91 (C), 115.72 (C), 113.83 (C), 113.31 (C), 56.21 (CH), 55.44 (CH<sub>3</sub>), 14.33 (CH<sub>3</sub>); <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  -114.06 (m); HRMS (ESI) Exact mass calcd for C<sub>16</sub>H<sub>17</sub>FNOS [M+H]<sup>+</sup>: 290.10100, found: 290.10094.

### ***N*-(1-Phenylethyl)piperidine (62)**



General procedure B was applied to styrene (115  $\mu$ L, 1 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (1.0 mg, 0.005 mmol), TMEDA (0.75  $\mu$ L, 0.005 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.5 mL, 1.5 mmol) and *O*-benzoyl-*N*-hydroxypiperidine **48** (328 mg, 1.6 mmol) added as a solution in THF (2.3 mL) over 1 h at 0 °C. The crude reaction mixture was quenched with sat. aq. NaHCO<sub>3</sub> (10 mL) and Et<sub>2</sub>O (10 mL). The aqueous phase was extracted with Et<sub>2</sub>O (3  $\times$  10 mL) and the combined organic phases then extracted with 1 M HCl (3  $\times$  10 mL). NaOH pellets were then added until the solution was strongly basic. The aqueous phase was then extracted with Et<sub>2</sub>O (3  $\times$  10 mL), dried and concentrated *in vacuo* to give **62** as a pale yellow oil (87.5 mg, 46%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.33-7.29 (4H, m, ArH), 7.26-7.21 (1H, m, ArH), 3.40 (1H, q,  $J$  = 6.8 Hz, CHCH<sub>3</sub>), 2.45-2.31 (4H, m, CH<sub>2</sub>), 1.59-1.53 (4H, m, CH<sub>2</sub>), 1.43-1.36 (5H, m, CH<sub>2</sub> + CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  144.0 (C), 128.0 (2  $\times$  CH), 127.7 (2  $\times$  CH), 126.6 (CH), 65.2 (CH), 51.5 (2  $\times$  CH<sub>2</sub>), 26.3 (2  $\times$  CH<sub>2</sub>), 24.6 (CH<sub>3</sub>), 19.4 (CH<sub>2</sub>). Data consistent with literature values.<sup>104</sup>

### **1-Methoxy-3-[1-(phenylsulfanyl)ethyl]benzene (63) and 1-methoxy-3-[2-(phenylsulfanyl)ethyl]benzene (64)**



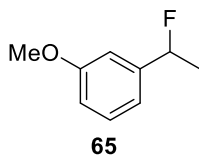
General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (0.14 mL, 1 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (1.0

mg, 0.005 mmol), TMEDA (0.7  $\mu$ L, 0.005 mmol) and ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 0.5 mL, 1.5 mmol). The reaction mixture was added to a solution of diphenyl sulphide **49** (349 mg, 1.6 mmol) in THF (2 mL) at  $-78^{\circ}\text{C}$  *via* cannula. The crude product was purified by flash chromatography (pentane $\rightarrow$ pentane/Et<sub>2</sub>O 98.8:1.2) to give a 10:1  $\alpha$ : $\beta$  inseparable mixture of **63** and **64** as a colourless oil (153 mg, 63%). *R*<sub>f</sub> 0.53 (pentane/Et<sub>2</sub>O 98:2);  $\nu_{\text{max}}/\text{cm}^{-1}$  3057, 2965, 2924, 2833, 1599, 1584, 1481, 1454, 1437, 1315; HRMS (ES) Exact mass calcd for C<sub>15</sub>H<sub>16</sub>OSNa [M+Na]<sup>+</sup>: 267.0814, found: 267.0816.

**63**: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.34-7.29 (2H, m, ArH), 7.26-7.17 (4H, m, ArH), 6.93-6.89 (1H, m, ArH), 6.89 (1H, t, *J* = 2.0 Hz, ArH), 6.77 (1H, ddd, *J* = 8.0, 2.5, 1.0 Hz, ArH), 4.32 (1H, q, *J* = 7.0 Hz, CHCH<sub>3</sub>), 3.77 (3H, s, OCH<sub>3</sub>), 1.63 (3H, d, *J* = 7.0 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  159.6 (C), 144.9 (C), 135.2 (C), 132.4 (C), 129.3 (C), 128.6 (C), 127.1 (C), 119.6 (C), 112.8 (2  $\times$  C), 112.6 (2  $\times$  C), 55.1 (CH<sub>3</sub>), 48.0 (CH), 22.3 (CH<sub>3</sub>);

**64**: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.39-7.16 (6H, m, ArH), 6.93-6.73 (3H, m, ArH), 3.80 (3H, s, OCH<sub>3</sub>), 3.21-3.15 (2H, m, CH<sub>2</sub>SPh), 2.92 (2H, dd, *J* = 9.0, 6.5 Hz, CH<sub>2</sub>CH<sub>2</sub>SPh); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  141.8 (C), 136.3 (C), 132.6 (C), 129.5 (C), 129.2 (C), 128.9 (C), 126.0 (C), 120.8 (C), 114.3 (2  $\times$  C), 111.7 (2  $\times$  C), 55.1 (CH<sub>3</sub>), 35.7 (CH<sub>2</sub>), 35.0 (CH<sub>2</sub>).

### 1-(1-Fluoroethyl)-3-methoxybenzene (**65**)

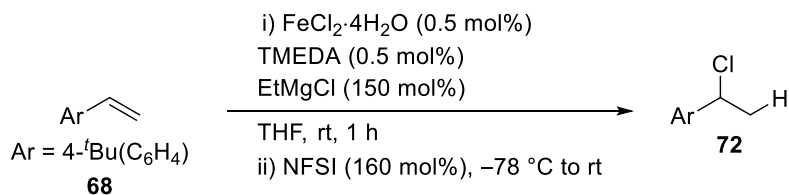


General procedure B was applied to 3-methoxy-1-vinylbenzene **28** (0.28 mL, 2.0 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (2.0 mg, 0.01 mmol), TMEDA (1.5  $\mu$ L, 0.01 mmol), ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 1.0 mL, 3 mmol) and NFSI **50** (1.01g, 3.2 mmol). The crude product was purified by flash chromatography (pentane/Et<sub>2</sub>O 99:1) to give **65** as a colourless oil (133 mg, 43%). *R*<sub>f</sub> 0.28 (pentane/Et<sub>2</sub>O 99:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  2983, 2936, 2837, 1603, 1587, 1489, 1457, 1436, 1289, 1261; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.34-7.28 (1H, m, ArH), 6.96-6.92 (2H, m, ArH), 6.90-6.86 (1H, m, ArH), 5.62 (1H, dq, *J* = 48.0, 6.5 Hz, CHF), 3.84 (3H, s, OCH<sub>3</sub>), 1.65 (3H, dd, *J* = 24.0, 6.5 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>)  $\delta$  159.7 (C), 143.1 (d, <sup>2</sup>*J*<sub>C-F</sub> = 19.5 Hz, C), 129.5 (CH), 117.4 (d, <sup>3</sup>*J*<sub>C-F</sub> = 6.5 Hz, CH), 113.6 (d, <sup>4</sup>*J*<sub>C-F</sub> = 2.0 Hz, CH), 110.7 (d, <sup>3</sup>*J*<sub>C-F</sub> = 7.5 Hz, CH), 90.8 (d, <sup>1</sup>*J*<sub>C-F</sub> = 168.0 Hz, CH), 55.2 (CH<sub>3</sub>), 22.9 (d, <sup>2</sup>*J*<sub>C-F</sub> = 25.0 Hz, CH<sub>3</sub>); <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>)  $\delta$  -176.7 (dq, *J* = 48.0 Hz, 24.0 Hz); HRMS (EI) Exact mass calcd for C<sub>9</sub>H<sub>11</sub>FO [M]<sup>+</sup>: 154.0788, found: 154.0786.

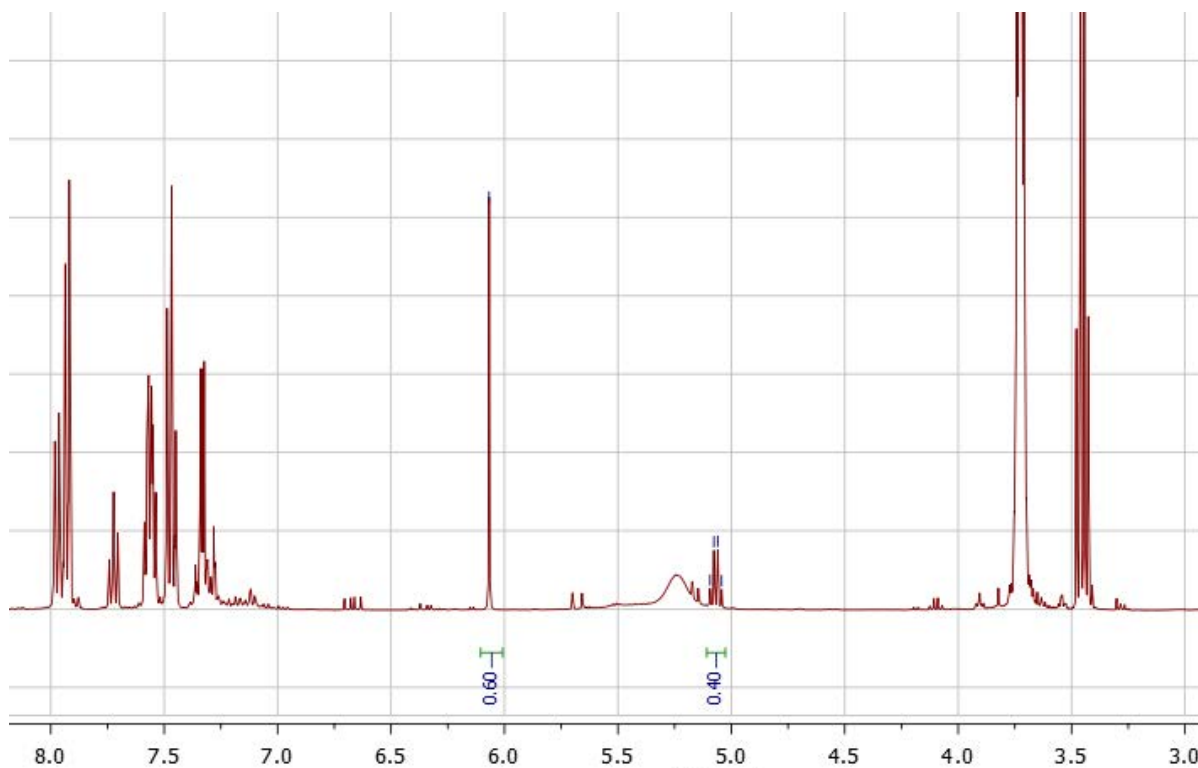


## 6.2.5: Hydromagnesiation using Different Halide Counter-ions (Table 3, p. 25)

### Reaction with ethylmagnesium chloride (Entry 1)



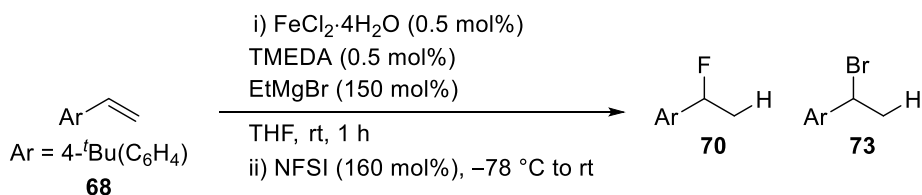
General procedure B was applied to 4-*tert*-butylstyrene **68** (65  $\mu$ L, 0.35 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (0.35 mg, 1.75  $\times 10^{-3}$  mmol), TMEDA (0.26  $\mu$ L, 1.75  $\times 10^{-3}$  mmol), ethylmagnesium chloride (2 M in THF, 0.26 mL, 0.53 mmol) and NFSI **50** (177 mg, 0.56 mmol).



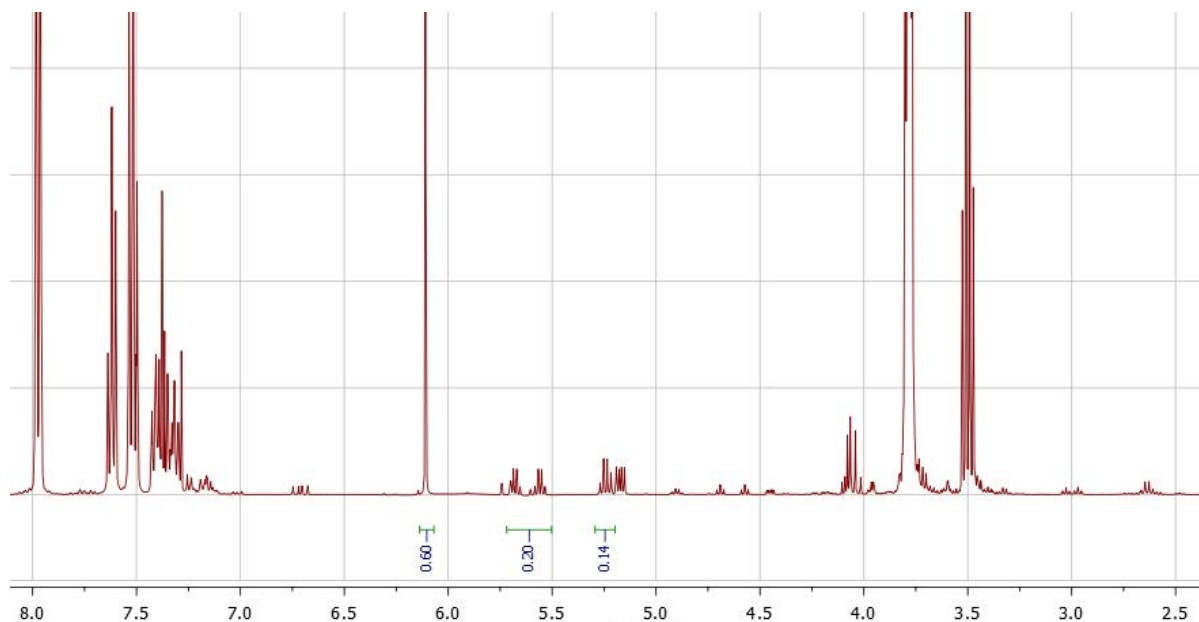
Trimethoxybenzene (20 mol%): 6.07 (s, 3H); 1-(1-chloroethyl)-4-*tert*-butylbenzene **72**: 5.07 (q,  $J = 6,8$  Hz, 1H) ppm;  $(0.40/1) \times 100 = 40\%$  yield.

Data was compared to similar products in the literature.<sup>105</sup>

### Reaction with ethylmagnesium bromide (Entry 2)



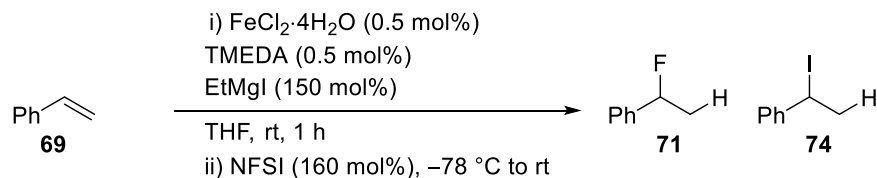
General procedure B was applied to 4-*tert*-butylstyrene **68** (65  $\mu\text{L}$ , 0.35 mmol),  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (0.35 mg,  $1.75 \times 10^{-3}$  mmol), TMEDA (0.26  $\mu\text{L}$ ,  $1.75 \times 10^{-3}$  mmol), ethylmagnesium chloride (3 M in  $\text{Et}_2\text{O}$ , 0.18 mL, 0.53 mmol) and NFSI **50** (177 mg, 0.56 mmol).



Trimethoxybenzene (20 mol%): 6.10 (s, 3H); 1-(1-fluoroethyl)-4-*tert*-butylbenzene **70**: 5.62 (dq,  $J = 47.8$ , 6.4 Hz, 1H) ppm;  $(0.20/1) \times 100 = 20\%$  yield; 1-(1-bromoethyl)-4-*tert*-butylbenzene **73**: 5.24 (q,  $J = 7.0$  Hz, 1H) ppm;  $(0.14/1) \times 100 = 14\%$  yield.

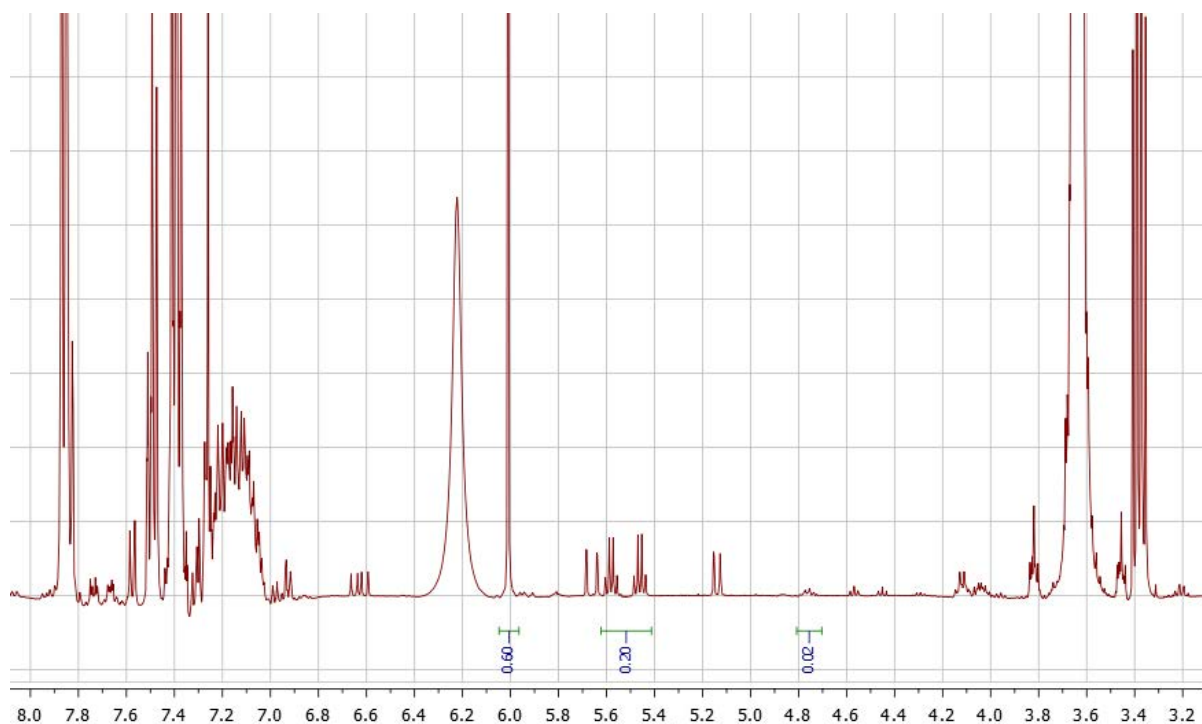
Data were consistent with literature values.<sup>106,107</sup>

### Reaction with ethylmagnesium iodide (Entry 3)



General procedure B was applied to styrene **69** (80  $\mu\text{L}$ , 0.7 mmol),  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (0.7 mg,  $3.5 \times 10^{-3}$  mmol), TMEDA (0.5  $\mu\text{L}$ ,  $3.5 \times 10^{-3}$  mmol), ethylmagnesium iodide (0.19 M in  $\text{Et}_2\text{O}$ , 5.7 mL, 1.05 mmol) and NFSI

**50** (353 mg, 1.12 mmol).

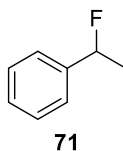


Trimethoxybenzene (20 mol%): 6.00 (s, 3H); (1-fluoroethyl)benzene **71**: 5.52 (dq,  $J = 47.7, 6.4$  Hz, 1H) ppm;  $(0.20/1) \times 100 = 20\%$  yield; 1-iodoethylbenzene **74**: 4.75 (q,  $J = 7.1$  Hz, 1H) ppm;  $(0.02/1) \times 100 = 2\%$  yield.

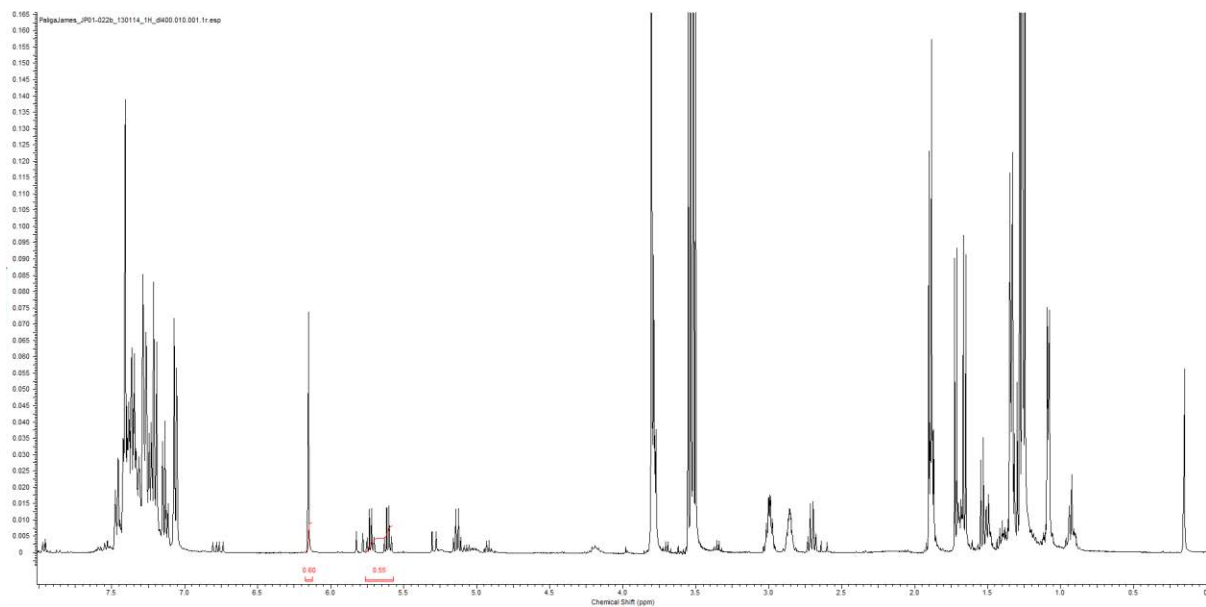
Data were consistent with literature values.<sup>108,109</sup>

## 6.2.6: Reactions of Preformed Grignard Reagents (Table 4, p. 26)

### (1-Fluoroethyl)benzene (**71**) (Entry 1)

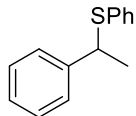


General procedure C was applied to 1-phenylethylmagnesium chloride **75** (0.11 M in THF, 8.8 mL, 1 mmol) and NFSI **50** (347 mg, 1.1 mmol). NFSI was added as a solution *via* cannula to the Grignard reagent at  $-78^{\circ}\text{C}$  and stirred for 16 h.

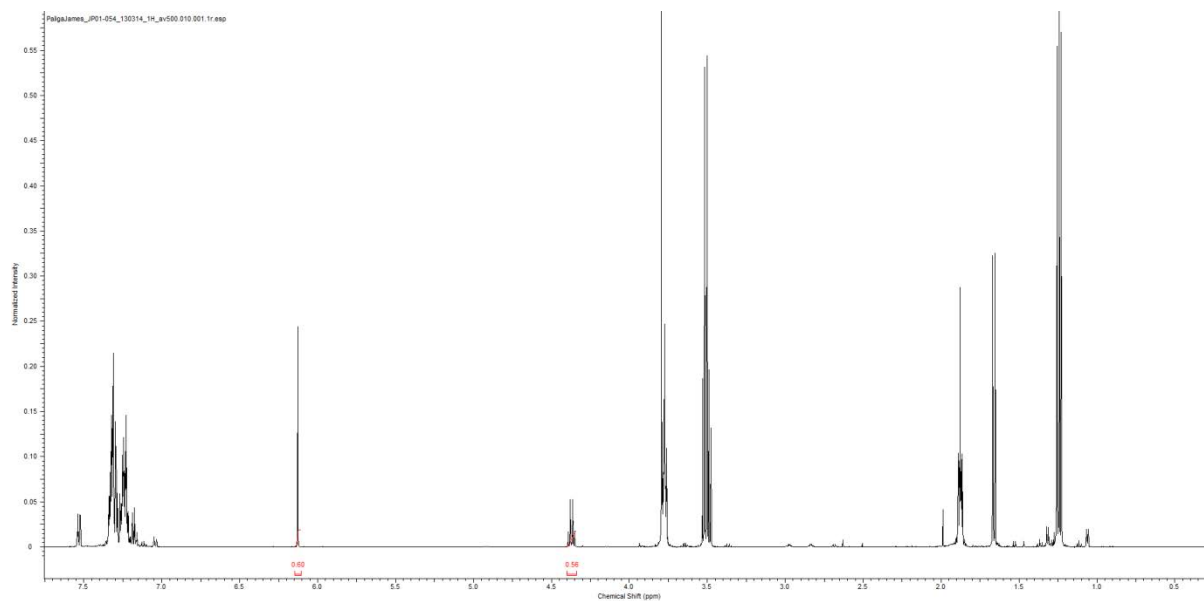


Trimethoxybenzene (20 mol%): 6.15 (s, 3H); (1-fluoroethyl)benzene **71**: 5.67 (dq,  $J = 47.6, 6.4$  Hz, 1H) ppm;  $(0.55/1) \times 100 = 55\%$ .

#### [(1-Phenylethyl)thio]benzene (Entry 5)

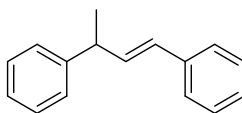


General procedure C was applied to 1-phenylethylmagnesium chloride **75** (0.31 M in THF, 2.26 mL, 0.7 mmol) and diphenyl disulphide **49** (245 mg, 1.1 mmol). Diphenyl disulphide **49** was added as a solution *via* cannula to the Grignard reagent at  $-78$  °C and stirred for 2 h.

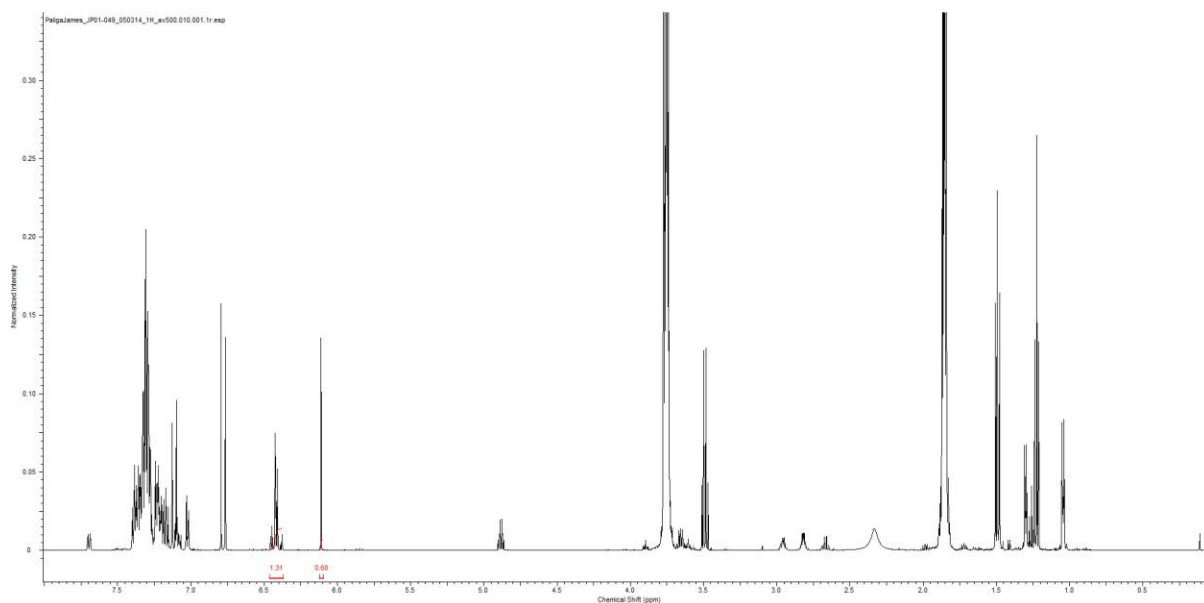


Trimethoxybenzene (20 mol%): 6.13 (s, 3H); [(1-phenylethyl)thio]benzene: 4.37 (q,  $J = 7.0$  Hz, 1H) ppm;  $(0.56/1) \times 100 = 56\%$ .

### 1,3-Diphenyl-1-butene (Entry 6)



General procedure C was applied to 1-phenylethylmagnesium chloride **75** (0.15 M in THF, 4.8 mL, 0.7 mmol), TMEDA (0.5  $\mu$ L, 0.0035 mmol) and  $\beta$ -bromostyrene **44** (0.14 mL, 1.1 mmol).  $\beta$ -Bromostyrene **44** was added dropwise to a solution of 1-phenylethylmagnesium chloride **75** and TMEDA and stirred for 2 hours.



Trimethoxybenzene (20 mol%): 6.11 (s, 3H); 1,3-diphenyl-1-butene: 6.42 (m, 2H) ppm;  $(1.31/2) \times 100 = 65\%$ .

## 6.2.7: Reactivity of Grignard Reagents with Electrophilic Nitrogen Reagent (Table 5, p. 28)

### Entry 1

General procedure C was applied to a solution of (1-phenylethyl)magnesium bromide **77** (0.94 M in Et<sub>2</sub>O, 0.53 mL, 0.5 mmol) in THF (1.1 mL) and a solution of *O*-benzoyl-*N*-hydroxypiperidine **48** (103 mg, 0.5 mmol) in THF (0.71 mL) to give amine **61** as a pale yellow oil (61%). Data was consistent with that previously reported.<sup>104</sup>

### Entry 2

General procedure C was applied to a solution of (1-phenylethyl)magnesium bromide **77** (0.94 M in Et<sub>2</sub>O, 0.53 mL, 0.5 mmol) and cyclopentylmagnesium bromide **78** (2 M in Et<sub>2</sub>O, 0.25 mL, 0.5 mmol) in THF (1.1 mL) and a solution of *O*-benzoyl-*N*-hydroxypiperidine **48** (51.3 mg, 0.25 mmol) in THF (0.36 mL) to give amine **61** as a pale yellow oil (70%). Data was consistent with that previously reported.<sup>104</sup>

### Entry 3

General procedure C was applied to a solution of (1-phenylethyl)magnesium bromide **77** (0.94 M in Et<sub>2</sub>O, 0.53 mL, 0.5 mmol), FeCl<sub>2</sub>·4H<sub>2</sub>O (0.5 mg,  $2.5 \times 10^{-3}$  mmol) and TMEDA (0.4 μL,  $2.5 \times 10^{-3}$  mmol) in

THF (1.1 mL) and a solution of *O*-benzoyl-*N*-hydroxypiperidine **48** (103 mg, 0.5 mmol) in THF (0.71 mL) to give amine **61** as a pale yellow oil (69%). Data was consistent with that previously reported.<sup>104</sup>

#### Entry 4

General procedure C was applied to a solution of (1-phenylethyl)magnesium bromide **77** (0.94 M in Et<sub>2</sub>O, 0.53 mL, 0.5 mmol), cyclopentylmagnesium bromide **78** (2 M in Et<sub>2</sub>O, 0.25 mL, 0.5 mmol) and 2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine iron (II) chloride<sup>99</sup> (15.2 mg, 0.025) in THF (0.37 mL) and a solution of *O*-benzoyl-*N*-hydroxypiperidine **48** (51.3 mg, 0.25 mmol) in THF (0.36 mL) to give amine **61** as an oil (63%). Data was consistent with that previously reported.<sup>104</sup>

## 6.2.8: Analysis of $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra to Determine Reactive Intermediate

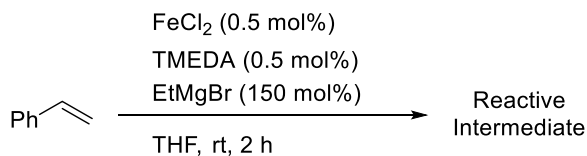
### Sample Preparation

$d_8$ -Tetrahydrofuran was distilled from sodium/benzophenone under reduced pressure.

Ethylmagnesium bromide (3 mmol, 1 M in THF, 3 mL) was added to an oven-dried Schlenk flask under a nitrogen atmosphere. The solvent was removed under reduced pressure to give a colourless solid.  $d_8$ -Tetrahydrofuran (0.5 mL) was added under a nitrogen atmosphere, and then removed under reduced pressure.  $d_8$ -Tetrahydrofuran (2.5 mL) was added to fully dissolve the colourless solid. The concentration of ethylmagnesium bromide was determined to be 0.9 M after titration against 2-hydroxybenzaldehyde phenylhydrazone.

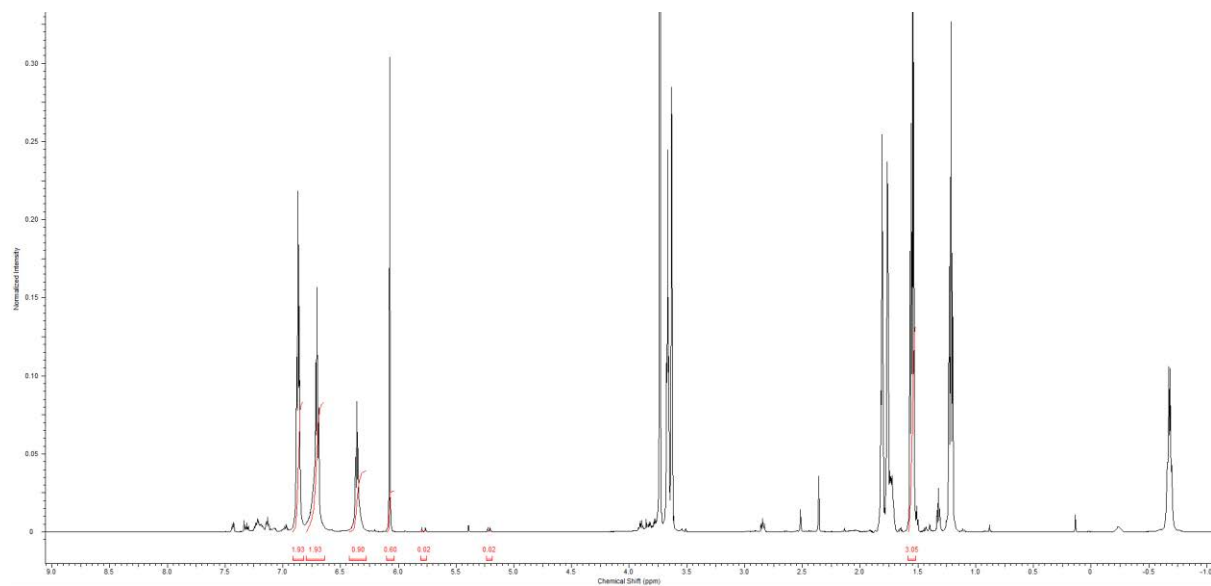
Cyclopentylmagnesium bromide in  $d_8$ -tetrahydrofuran was prepared in a similar manner to give a 1.1 M solution, based upon titration against 2-hydroxybenzaldehyde phenylhydrazone.

### Hydromagnesiation under Thomas conditions



Styrene **69** (16  $\mu\text{L}$ , 0.14 mmol),  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (0.14 mg,  $0.7 \times 10^{-3}$  mmol, 0.5 mol%), TMEDA (0.1  $\mu\text{L}$ ,  $0.7 \times 10^{-3}$  mmol, 0.5 mol%) and  $d_8$ -tetrahydrofuran (1 mL) were added to an oven-dried Schlenk flask under a nitrogen atmosphere. Ethylmagnesium bromide (0.22 mmol, 0.9 M in  $d_8$ -THF, 0.25 mL) was added and the reaction stirred for 2 hours. A 0.6 mL sample was removed and added to an oven-dried NMR tube fitted with a J. Young's valve under a nitrogen atmosphere.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded for Grignard reagent characterisation.





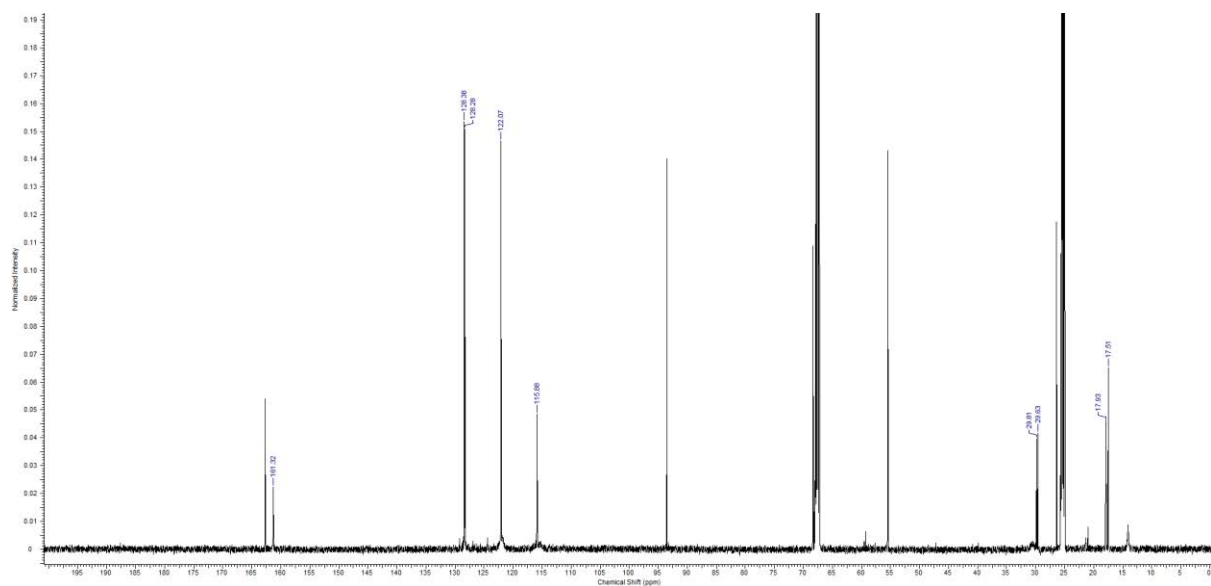
$^1\text{H}$  NMR Data (500 MHz,  $d_8$ -THF):

1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.07 (s, 3 H) ppm. Integral set to 0.6 ( $0.2/1 \times 3 \text{ H} = 0.6$ ).

(1-Phenylethyl)magnesium bromide **77**: 6.87 (br. app. t, 2 H, ArH), 6.70 (br. app. t, 2 H ArH), 6.36 (br. app. t, 1H, ArH), 1.55 (m, 3 H, CH<sub>3</sub>) ppm. > 95% conversion to Grignard reagent.

Styrene **69**: 5.78 (d,  $J = 17.6$  Hz, 1 H), 5.21 (d,  $J = 10.9$  Hz, 1 H) ppm.  $(0.02 \times 100)/1 = 2\%$  returned starting material.

Data was consistent with that previously reported.<sup>58</sup>



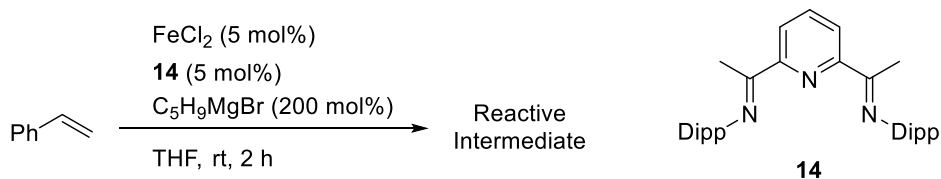
$^{13}\text{C}$  NMR Data (125.8 MHz,  $d_8$ -THF):

Peaks at 162.7, 93.5 and 55.5 ppm correspond to 1,3,5-trimethoxybenzene.

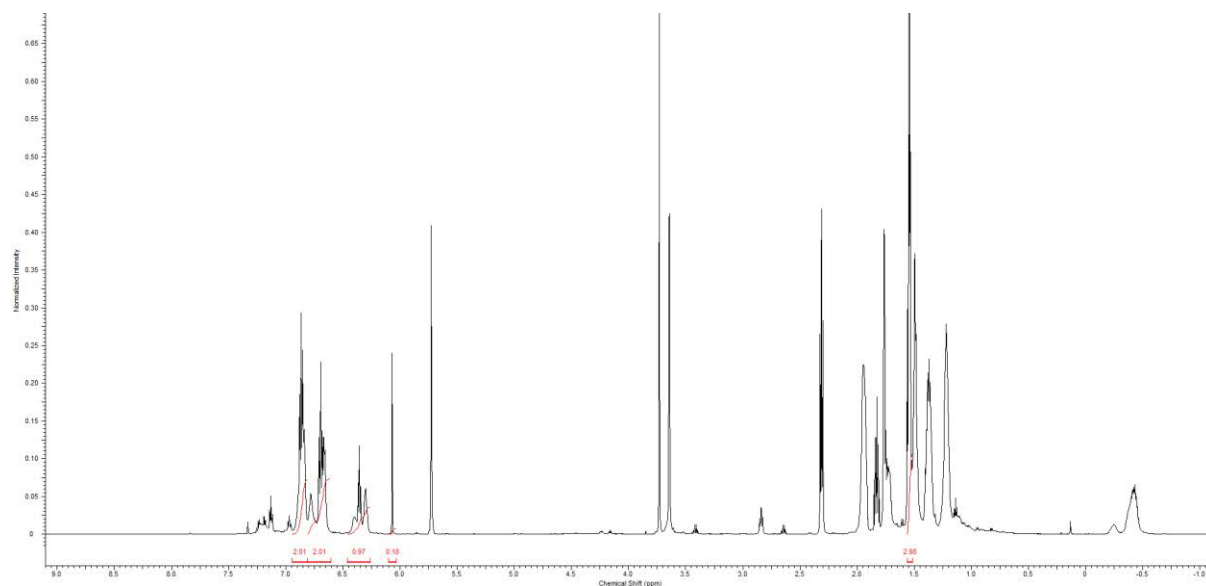
(1-Phenylethyl)magnesium bromide **77**: 161.3, 128.4, 128.3, 122.1, 115.9, 29.8, 29.6, 17.9, 17.5 ppm.

Data was consistent with that previously reported.<sup>58</sup>

### Hydromagnesiation under Yang conditions



Styrene **69** (27  $\mu\text{L}$ , 0.23 mmol), 2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine iron (II) chloride<sup>1</sup> (7 mg,  $11.5 \times 10^{-3}$  mmol, 5 mol%) and  $d_8$ -tetrahydrofuran (0.5 mL) were added to an oven-dried Schlenk flask under a nitrogen atmosphere. Cyclopentylmagnesium bromide **78** (0.46 mmol, 1.1 M in  $d_8$ -THF, 0.42 mL) was added and the reaction stirred for 2 hours. A 0.6 mL sample was removed and added to an oven-dried NMR tube fitted with a J. Young's valve under a nitrogen atmosphere.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded for Grignard reagent characterisation.



$^1\text{H}$  NMR Data (500 MHz,  $d_8$ -THF):

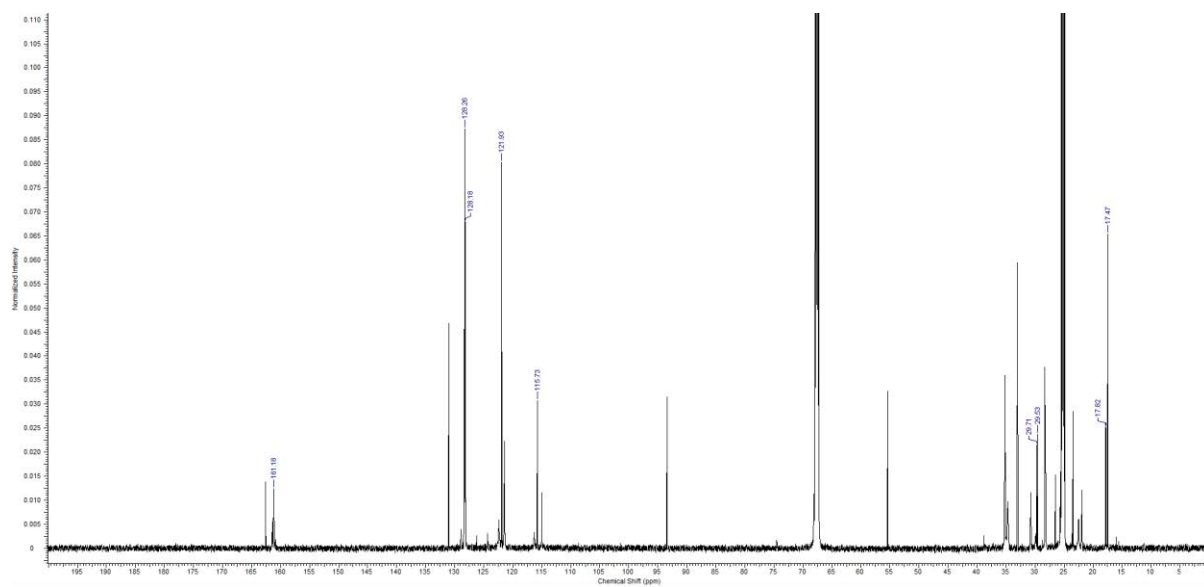
1,3,5-Trimethoxybenzene (6 mol%) used as internal standard: 6.07 (s, 3 H) ppm. Integral set to 0.18 (0.06/1  $\times$  3 H).

(1-Phenylethyl)magnesium bromide **77**: 6.86 (br. m, 2 H, ArH), 6.69 (br. m, 2 H, ArH), 6.35 (br. m, 1 H,

ArH), 1.55 (br. m, 3 H, CH<sub>3</sub>). ~100% conversion to Grignard reagent.

Data was consistent with that previously reported.<sup>58</sup>

The increased complexity of the aromatic proton signals may be attributed to an alkyl exchange between (1-phenylethyl)magnesium bromide **77** and the dialkyl magnesium species, bis(1-phenylethyl)magnesium and (1-phenylethyl)(cyclopentyl)magnesium.<sup>58</sup>



<sup>13</sup>C NMR Data (125.8 MHz, d<sub>8</sub>-THF):

Peaks at 162.6, 93.4 and 55.4 ppm correspond to 1,3,5-trimethoxybenzene.

(1-Phenylethyl)magnesium bromide **77**: 161.2, 128.3, 128.2, 121.9, 115.7, 29.7, 29.5, 17.8, 17.5 ppm.

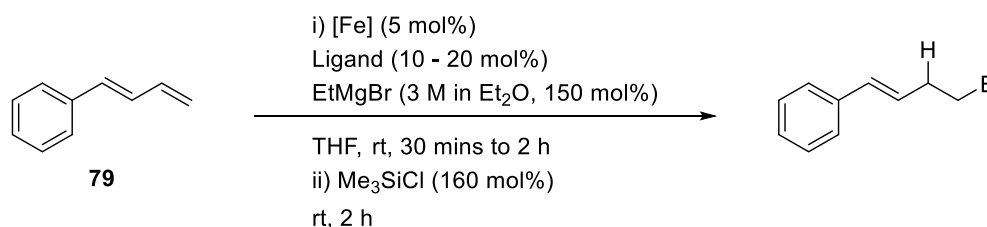
Additional signals may be attributed to dialkyl magnesium species, bis(1-phenylethyl)magnesium and (1-phenylethyl)(cyclopentyl)magnesium.<sup>58</sup>

Data was consistent with that previously reported.<sup>58</sup>

## 6.3: Iron-Catalysed Hydromagnesiation of a 1,3-Diene

### 6.3.1: General Procedures

#### General Procedure E: Hydrofunctionalisation of 1-phenyl-1,3-butadiene

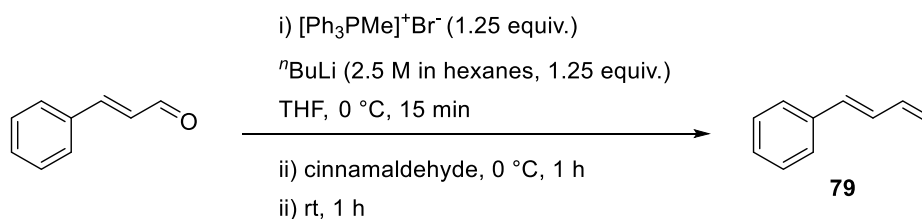


A solution of iron salt (5 mol%) and ligand (10-20 mol%) in anhydrous THF (3 mL) was prepared under nitrogen. To this, 1-phenyl-1,3-butadiene **79** (29.5  $\mu$ L, 0.21 mmol) was added to the flask and stirred for approx. 1 minute before ethylmagnesium bromide (3 M in Et<sub>2</sub>O, 110  $\mu$ L, 0.32 mmol) was added. The reaction was stirred for 2 h before chlorotrimethylsilane (43  $\mu$ L, 0.34 mmol) was added at room temperature. The reaction was stirred for a further 1 h and quenched with water (10 mL). The phases were separated and the aqueous phase extracted with Et<sub>2</sub>O (3  $\times$  5 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*.

Known products were identified by <sup>1</sup>H NMR spectroscopy and characterised by comparison with authentic samples of spectral data. Yields were calculated from <sup>1</sup>H NMR spectra using 1,3,5-trimethoxybenzene (20 mol%) as an internal standard.

## 6.3.2: Synthesis of 1,3-Dienes

### 1-Phenyl-1,3-butadiene (79)



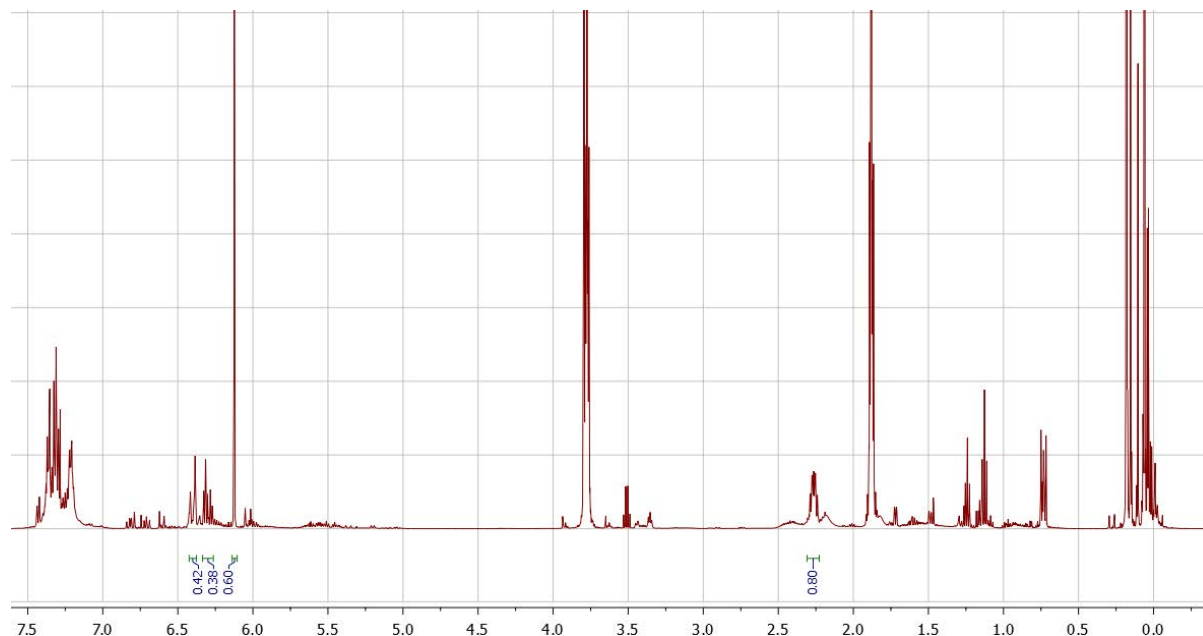
To a suspension of methyltriphenylphosphonium bromide (7.14 g, 20 mmol) in THF (100 mL) at 0 °C under nitrogen, *n*-butyllithium (2.5 M in hexanes, 8 mL, 20 mmol) was added slowly *via* a drop-wise addition and the mixture was stirred for 15 minutes. A solution of cinnamaldehyde (2 mL, 16 mmol) in THF (20 mL) was then added and stirred for a further 1 h. The reaction mixture was then warmed to room temperature and stirred for an additional 1 h then quenched with a saturated solution of  $\text{NH}_4\text{Cl}$  (100 mL). The phases were separated and the aqueous phase extracted with  $\text{Et}_2\text{O}$  ( $3 \times 100$  mL). The combined organic extracts were washed with brine (100 mL), dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The resulting residue was then applied to a plug of silica, eluted with hexane and the solvent removed *in vacuo* to give 1-phenyl-1,3-butadiene **79** (1.48 g, 71%) as a yellow oil.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (2 H, d,  $J = 7.2$  Hz, ArH), 7.35-7.31 (2 H, m, ArH), 7.26-7.22 (1 H, m, ArH), 6.80 (1 H, dd,  $J = 15.6, 10.5$  Hz, ArCH=CHCH=CH<sub>2</sub>), 6.60-6.48 (2 H, m, ArCH=CHCH=CH<sub>2</sub>), 5.35 (1 H, d,  $J = 16.9$  Hz, ArCH=CHCH=CH<sub>2</sub>), 5.19 (1 H, d,  $J = 10.0$  Hz, ArCH=CHCH=CH<sub>2</sub>);  $^{13}\text{C}$  NMR (125.8 MHz,  $\text{CDCl}_3$ )  $\delta$  137.33, 137.29, 133.01, 129.78, 128.75, 127.77, 126.59, 117.73. Data consistent with literature.<sup>110</sup>

### 6.3.3: Reaction Screening

#### Initial 1,3-diene Hydromagnesiation Catalyst Screen (Table 6, p. 30)

##### Entry 1

General procedure E was applied to iron(II) chloride tetrahydrate (7 mg, 0.035 mmol), TMEDA (5  $\mu$ L, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu$ L, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL).



$^1\text{H}$  NMR Data (500 MHz,  $\text{CDCl}_3$ ):

1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.12 ppm (s, 3 H). Integral set to 0.6 (0.2/1  $\times$  3H = 0.6).

(*E*)-Trimethyl(4-phenylbut-3-enyl)silane **80**: 6.41 (d,  $J$  = 15.8 Hz, 1 H, ArCH=CH), 6.30 (dt,  $J$  = 15.9, 6.5 Hz, 1 H, ArCH=CH), 2.31 – 2.23 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>Si) ppm.

The yield of 1,2-hydrosilylation product **80** was determined to be 40%. Data was consistent with literature values.<sup>111</sup>

##### Entry 2

General procedure E was applied to iron(III) acetylacetonate (12.4 mg, 0.035 mmol), TMEDA (5  $\mu$ L, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu$ L, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL). The yield of 1,2-hydrosilylated product **80** was determined to be 35%. Data was consistent with literature values.<sup>111</sup>

### Entry 3

General procedure E was applied to <sup>Et</sup>BIPFeCl<sub>2</sub> complex (21 mg, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98 μL, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL). Upon analysis of the <sup>1</sup>H NMR it appeared that the majority of the starting material had polymerised.

### Entry 4

General procedure E was applied to cyclohexyliminopyridineiron(II) chloride complex (11 mg, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98 μL, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL). The yield of 1,2-hydrosilylated product **80** was determined to be 34%. Data was consistent with literature values.<sup>111</sup>

### Entry 5

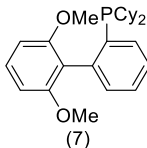
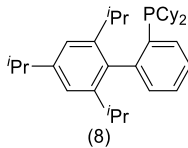
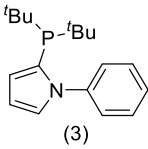
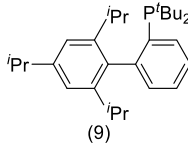
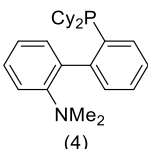
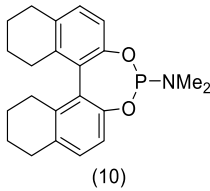
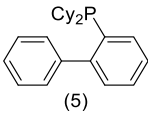
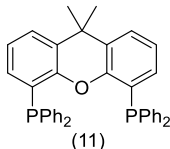
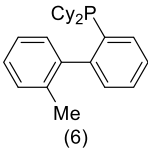
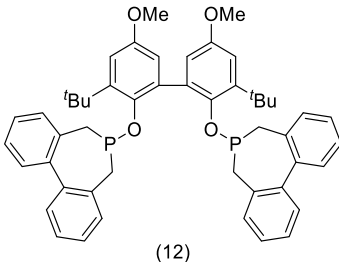
General procedure E was applied to *tert*-butyliminopyridineiron(II) chloride complex (10 mg, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98 μL, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL). The yield of 1,2-hydrosilylated product **80** was determined to be 34%. Data was consistent with literature values.<sup>111</sup>

### Entry 6

General procedure E was applied to di-*iso*-propylphenyliminopyridineiron(II) chloride complex (10 mg, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98 μL, 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.02 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (5 mL). Upon analysis of the <sup>1</sup>H NMR it appeared that the majority of the starting material had polymerised.

# In-depth Catalyst and Ligand Screen for Diene Hydromagnesiation

Table of Iron Salts and Ligands Used

Iron Salt	Ligand	
FeCl <sub>2</sub> (A)	P(CH <sub>2</sub> CH <sub>2</sub> CN) <sub>3</sub> (1)	 (7)
Fe(acac) <sub>2</sub> (B)	P(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (2)	 (8)
Fe(stearate) <sub>2</sub> (C)	 (3)	 (9)
Fe(BF <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O (D)	 (4)	 (10)
FeBr <sub>2</sub> (E)	 (5)	 (11)
FeCl <sub>2</sub> + TMEDA (F)	 (6)	 (12)

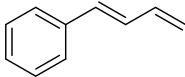
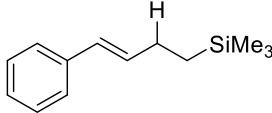
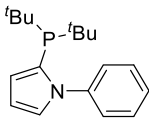
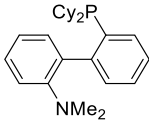
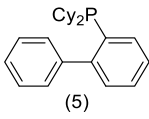
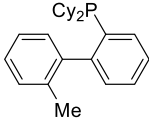
For all of the combinations of iron salt and ligand, general procedure E was followed:

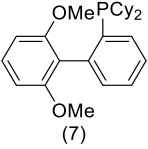
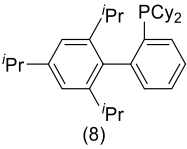
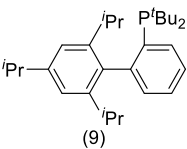
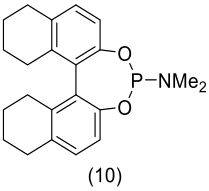
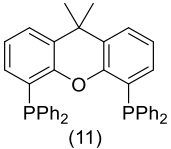
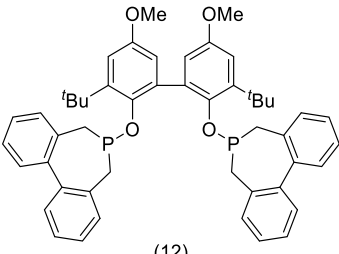
A – 1.33 mg, 0.011 mmol; B – 2.67 mg, 0.011 mmol; C – 6.54 mg, 0.011 mmol; D – 3.54 mg, 0.011 mmol; E – 2.26 mg, 0.011 mmol; F – (0.5 mL taken from a solution of FeCl<sub>2</sub> (13.3 mg, 0.11 mmol) and TMEDA (16 μL, 0.11 mmol)).



1 – 8.11 mg, 0.042 mmol; 2 – 22.4 mg, 0.042 mmol; 3 – 12.1 mg, 0.042 mmol; 4 – 16.5 mg, 0.042 mmol; 5 – 14.7 mg, 0.042 mmol; 6 – 15.3 mg, 0.042 mmol; 7 – 17.2 mg, 0.042 mmol; 8 – 20.0 mg, 0.042 mmol; 9 – 17.8 mg, 0.042 mmol; 10 – 15.4 mg, 0.042 mmol; 11 – 12.2 mg, 0.021 mmol; 12 – 16.5 mg, 0.021 mmol.

## Results of Catalyst Screen

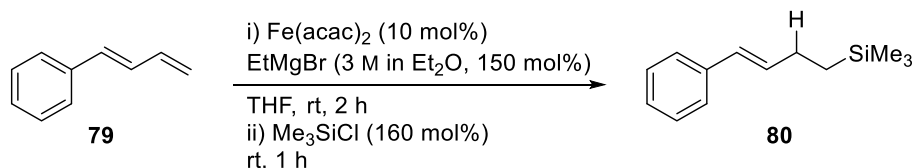
<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;">  <p><b>79</b></p> </div> <div style="text-align: center;"> <p>i) [Fe] (5 mol%) Ligand (10 - 20 mol%) EtMgBr (3 M in Et<sub>2</sub>O, 150 mol%)</p> <hr style="width: 100%;"/> <p>THF, rt, 30 mins to 2 h ii) Me<sub>3</sub>SiCl (160 mol%) rt, 2 h</p> </div> <div style="text-align: center;">  <p><b>80</b></p> </div> </div>					
		FeCl <sub>2</sub> (A)	Fe(acac) <sub>2</sub> (B)	Fe(stearate) <sub>2</sub> (C)	Fe(BF <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O (D)
Entry	Ligand	A (%) <sup>a</sup>	B (%) <sup>a</sup>	C (%) <sup>a</sup>	D (%) <sup>a</sup>
<b>1<sup>b,c</sup></b>	P(CH <sub>2</sub> CH <sub>2</sub> CN) <sub>3</sub> (1)	-	-	5	-
<b>2<sup>b,c</sup></b>	P(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (2)	-	-	20	15
<b>3<sup>b,c</sup></b>	 (3)	-	23	25	23
<b>4<sup>b</sup></b>	 (4)	25	32	33	34
<b>5<sup>b</sup></b>	 (5)	20	28	34	14
<b>6<sup>b</sup></b>	 (6)	27	32	36	19

<b>7<sup>b</sup></b>	 (7)	20	n/a <sup>d</sup>	32	22
<b>8<sup>b</sup></b>	 (8)	26	30	42	10
<b>9<sup>b</sup></b>	 (9)	25	30	33	25
<b>10<sup>b,c</sup></b>	 (10)	-	-	-	-
<b>11<sup>e</sup></b>	 (11)	23	29	28	14
<b>12<sup>e</sup></b>	 (12)	5	6	11	7
<b>13</b>	None	20	28	n/a <sup>f</sup>	15

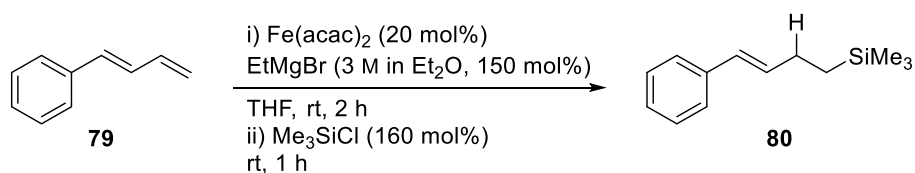
<sup>a</sup> Yields were calculated by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. <sup>b</sup> 20 mol% ligand used. <sup>c</sup> Reactions ran at an elevated temperature. <sup>d</sup> No internal standard was added. <sup>e</sup> 10 mol% ligand used. <sup>f</sup> Fe(stearate)<sub>2</sub> was insoluble in the absence of ligand.

## 6.3.4: Probing Reaction Conditions

### Increased Catalyst Loading

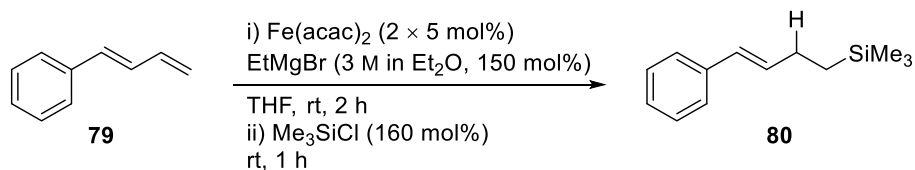


General procedure E was applied to  $\text{Fe}(\text{acac})_2$  (18 mg, 0.07 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ , 0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.05 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (10 mL). The product **80** was obtained in 40% yield. Data was compared to literature values.<sup>111</sup>



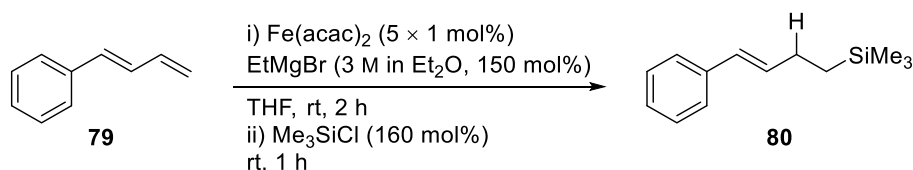
General procedure E was applied to  $\text{Fe}(\text{acac})_2$  (35.6 mg, 0.14 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ , 0.7 mmol), ethylmagnesium bromide (0.47 mL, 1.4 mmol), chlorotrimethylsilane (0.2 mL, 1.54 mmol) and THF (20 mL). The product **80** was obtained in 38% yield. Data was compared to literature values.<sup>111</sup>

### Addition of Catalyst in Multiple Portions



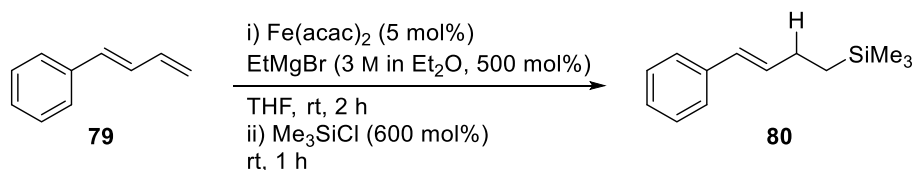
A solution of  $\text{Fe}(\text{acac})_2$  (8.9 mg, 0.035 mmol) in anhydrous THF (10 mL) was prepared under nitrogen. To this, 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ , 0.7 mmol) was added to the flask and stirred for approx. 1 minute before ethylmagnesium bromide (3 M in  $\text{Et}_2\text{O}$ , 0.35 mL, 1.05 mmol) was added. The reaction was stirred for 30 minutes before a second portion of  $\text{Fe}(\text{acac})_2$  (8.9 mg, 0.035 mmol) in anhydrous THF (10 mL) was added. The reaction was stirred for another 1.5 h before chlorotrimethylsilane (0.14 mL, 1.12 mmol) was added. The reaction was stirred for a further 1 hour and quenched with water (10 mL). The phases were separated and the aqueous phase extracted with  $\text{Et}_2\text{O}$  (3  $\times$  5 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo* to give the product **80** in a 50% yield determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an

internal standard. Data was consistent with literature values.<sup>111</sup>



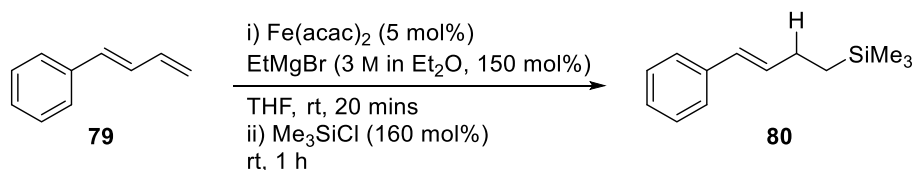
A solution of  $\text{Fe}(\text{acac})_2$  (1.78 mg, 0.007 mmol) in anhydrous THF (10 mL) was prepared under nitrogen. To this, 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ , 0.7 mmol) was added to the flask and stirred for approx.. 1 minute before ethylmagnesium bromide (3 M in  $\text{Et}_2\text{O}$ , 0.35 mL, 1.05 mmol) was added. Following this, every 20 minutes a portion of  $\text{Fe}(\text{acac})_2$  (1.78 mg, 0.007 mmol) was added to the reaction mixture until five portions had been added in total. After stirring for 2 hours, chlorotrimethylsilane (0.14 mL, 1.12 mmol) was added and the reaction stirred for a further 1 hour. The reaction was quenched with water (10 mL), the phases separated and the aqueous phase extracted with  $\text{Et}_2\text{O}$  ( $3 \times 5$  mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo* to give the product **80** in a 46% yield determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>111</sup>

### Excess of Grignard Reagent and Electrophile



General procedure E was applied to  $\text{Fe}(\text{acac})_2$  (8.9 mg, 0.7 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ , 0.7 mmol), ethylmagnesium bromide (1.2 mL, 3.5 mmol), chlorotrimethylsilane (0.53 mL, 4.2 mmol) and THF (10 mL). The product **80** was obtained in 25% yield. Data was consistent with literature values.<sup>111</sup>

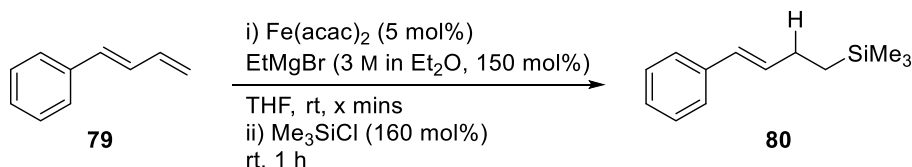
### Hydromagnesiation Reaction Length



General procedure E was applied to  $\text{Fe}(\text{acac})_2$  (8.9 mg, 0.035 mmol), 1-phenyl-1,3-butadiene **79** (98  $\mu\text{L}$ ,

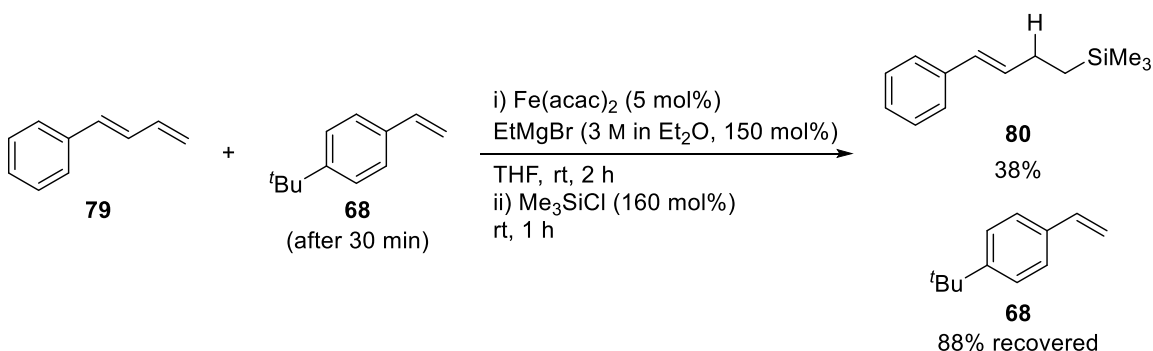
0.7 mmol), ethylmagnesium bromide (0.35 mL, 1.05 mmol), chlorotrimethylsilane (0.14 mL, 1.12 mmol) and THF (10 mL). Chlorotrimethylsilane was added after 30 minutes of stirring the reaction mixture with ethylmagnesium bromide. The product **80** was obtained in 36% yield. Data was consistent with literature values.<sup>111</sup>

### Determining the End Point (Table 7, p. 33)



To a solution of Fe(acac)<sub>2</sub> (8.9 mg, 0.035 mmol) and 1-phenyl-1,3-butadiene (98  $\mu$ L, 0.7 mmol) in THF (10 mL), ethylmagnesium bromide (0.35 mL, 1.05 mmol) was added and the reaction stirred. In a separate flask, a solution of chlorotrimethylsilane (0.14 mL, 1.12 mmol) and 1,3,5-trimethoxybenzene (23.5 mg, 0.14 mmol) in THF (10 mL) was prepared and aliquots of 0.5 mL of this solution were added into vials equipped with stirrer bars and sealed under nitrogen. After allotted time periods, 0.5 mL of reaction mixture was added to a pre-prepared vial and stirred for 1 hour before being quenched with water (1 mL). The yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. Data was consistent with literature values.<sup>111</sup>

### Competition Reaction Between 1-Phenyl-1,3-butadiene and 4-*tert*-Butylstyrene



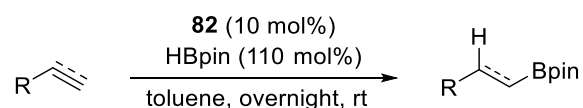
To a solution of Fe(acac)<sub>2</sub> (8.9 mg, 0.035 mmol) and 1-phenyl-1,3-butadiene **79** (98  $\mu$ L, 0.7 mmol) in THF (10 mL), ethylmagnesium bromide (0.35 mL, 1.05 mmol) was added. After stirring the reaction mixture for 30 minutes, 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol) was added and the reaction mixture stirred for a further 90 minutes before chlorotrimethylsilane (0.14 mL, 1.12 mmol) was added. The reaction was stirred for a further 1 h and quenched with water (10 mL). The phases were separated and the aqueous phase

extracted with Et<sub>2</sub>O (3 × 5 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (MgSO<sub>4</sub>) and the solvent removed *in vacuo*. The hydrosilylation product of the 1,3-diene, **80**, was determined to be 38% by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. Using the same methods, 88% of the 4-*tert*-butylstyrene starting material **68** was found to be remaining. Data were consistent with literature values.<sup>111,112</sup>

## 6.4: Magnesium-catalysed Hydrosilylation and Hydroboration

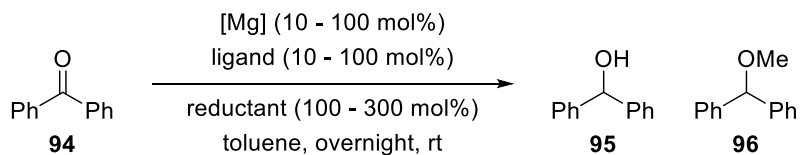
### 6.4.1: General Procedures

#### General Procedure F: Hydroboration of alkenes and alkynes



To a solution of alkene/alkyne (2 mmol) in toluene (2.5 mL), the magnesium complex **82** (3.6 mL, 0.2 mmol) was added. To this, pinacol borane (0.3 mL, 2.05 mmol) was then added dropwise and the reaction mixture was left to stir overnight at room temperature. The mixture was then quenched with water and the aqueous layer extracted with Et<sub>2</sub>O (3 × 5 mL). The combined organic layers were then dried over MgSO<sub>4</sub> and the solvent removed *in vacuo* to give the product. Yields were determined from <sup>1</sup>H NMR spectra using 1,3,5-trimethoxybenzene (20 mol%) as an internal standard.

#### General Procedure G: Reduction of benzophenone

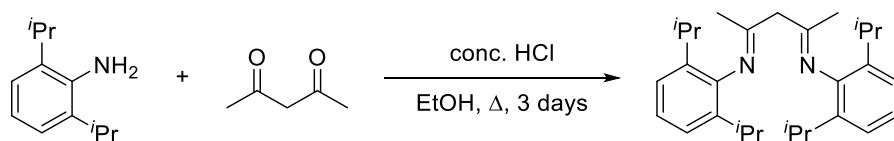


To a solution of benzophenone (91.1 mg, 0.5 mmol) in toluene (2 mL), [Mg] (10-100 mol%) and ligand (10-100 mol%) were added. To this, reductant (phenylsilane or pinacol borane, 100-300 mol%) was then added dropwise and the reaction mixture was left to stir overnight at room temperature. The mixture was then hydrolysed by one of two methods: A - methanol (5 mL) and aqueous NaOH (6 M, 2 mL) and left to stir for 1 h; or B – methanol (5 mL) and aqueous HCl (1 M, 2 mL) and refluxed for 1 h. The aqueous layer was then extracted with Et<sub>2</sub>O (3 × 5 mL) and the combined organic layers washed with brine (5 mL) before being dried over MgSO<sub>4</sub>. The solvent was removed *in vacuo* to give the products. Yields were determined from <sup>1</sup>H NMR spectra using 1,3,5-trimethoxybenzene (20 mol%) as an internal standard.

## 6.4.2: Synthesis of Ligands and Complexes

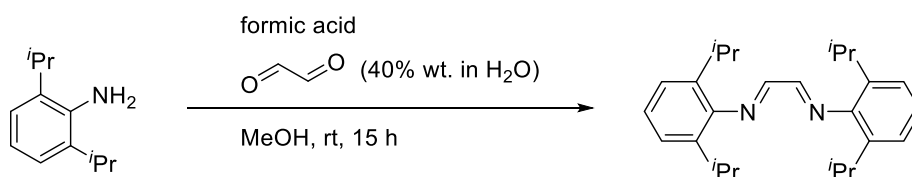
### Synthesis of Ligands

#### *N,N'*-Bis(2,6-diisopropylphenyl)pentane-2,4-diimine “Nacnac”



To a solution of 2,6-diisopropylaniline (23 mL, 110 mmol) and acetylacetone (5.13 mL, 50 mmol) in ethanol (200 mL), concentrated hydrochloric acid (4.1 mL, 49 mmol) was added. The reaction mixture was then heated at reflux for 3 days. The crude product was then extracted with dichloromethane, washed with  $\text{NaHCO}_3$  solution and the organic layer separated. The solvent was then removed *in vacuo* and the resulting solid was recrystallised from methanol to give the product as a white crystalline solid (9.42 g, 45 %).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  12.11 (1H, s,  $\text{NH}$ ), 7.13 (6H, m,  $\text{ArH}$ ), 4.88 (1H, s,  $\text{C}=\text{CH}$ ), 3.13 (4H, sept,  $J = 6.86$  Hz,  $\text{CH}(\text{CH}_3)_2$ ), 1.72 (6H, s,  $\text{CH}_3$ ), 1.23 (12H, d,  $J = 6.94$  Hz,  $\text{CH}(\text{CH}_3)_2$ ), 1.13 (12H, d,  $J = 6.86$  Hz,  $\text{CH}(\text{CH}_3)_2$ ).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.34 ( $2 \times \text{C}$ ), 142.61 ( $2 \times \text{C}$ ), 140.87 ( $4 \times \text{C}$ ), 125.22 ( $2 \times \text{CH}$ ), 123.16 ( $4 \times \text{CH}$ ), 93.37 ( $\text{CH}_2$ ), 28.33 ( $4 \times \text{CH}$ ), 24.36 ( $2 \times \text{CH}_3$ ), 23.36 ( $4 \times \text{CH}_3$ ), 20.90 ( $4 \times \text{CH}_3$ ). Data consistent with literature.<sup>113</sup>

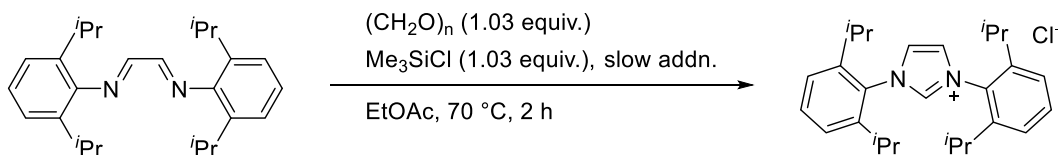
#### 1,2-Bis(2,6-diisopropylphenylimino)ethane



To a solution of 2,6-diisopropylaniline (9.43 mL, 50 mmol) in methanol (25 mL), glyoxal (40% wt in  $\text{H}_2\text{O}$ , 2.9 mL, 25 mmol) was added, followed by a drop of formic acid. The reaction mixture was then stirred at room temperature for 15 h. The reaction mixture was then filtered and the filtrate washed with methanol ( $3 \times 20$  mL) and dried *in vacuo* to give the final product as a yellow crystalline solid (6.7 g, 72%).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.11 (2H, s,  $\text{N}=\text{CH}$ ), 7.19 (6H, m,  $\text{ArH}$ ), 2.95 (4H, sept,  $J = 6.94$  Hz,  $\text{CH}(\text{CH}_3)_2$ ), 1.22 (24H, d,  $J = 6.86$  Hz,  $\text{CH}(\text{CH}_3)_2$ );  $^{13}\text{C}$  NMR (125.8 MHz,  $\text{CDCl}_3$ )  $\delta$  163.25 ( $2 \times \text{CH}$ ), 148.17 ( $2 \times \text{C}$ ), 136.87 ( $4 \times \text{C}$ ), 125.27 ( $2 \times \text{CH}$ ), 123.33 ( $4 \times \text{CH}$ ), 28.20 ( $4 \times \text{CH}$ ), 23.53 ( $8 \times \text{CH}_3$ ). Data consistent with literature.<sup>114</sup>

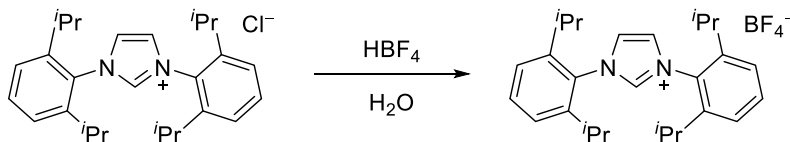


### 1,3-Bis(2,6-diisopropylphenyl)imidazolium chloride



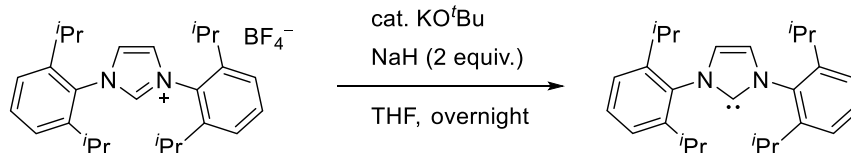
A solution of 1,2-bis(2,6-diisopropylphenyl)ethane (6.7 g, 17.9 mmol) and paraformaldehyde (0.54 mg, 18 mmol) in ethyl acetate (161 mL) was heated to 70 °C. To this, a solution of trimethylsilyl chloride (2.3 mL, 18 mmol) in ethyl acetate (2.4 mL) was added over 5 minutes. The reaction mixture was stirred for a further 2 h at 70 °C. The mixture was then cooled to 10 °C before being filtered and washed with ethyl acetate. The solvent was then removed *in vacuo* to give the product as an amorphous off-white solid (6.63 g, 87%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 10.17 (1H, s, NC(H)N), 8.15 (2H, s, NC=CH), 7.58 (2H, t, *J* = 7.86 Hz, ArH), 7.37 (4H, d, *J* = 7.86 Hz, ArH), 2.47 (4H, sept, *J* = 6.82 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.31 (12H, d, *J* = 6.82 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.27 (12H, d, *J* = 6.82 Hz, CH(CH<sub>3</sub>)<sub>2</sub>). <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 145.20 (CH), 138.99 (2 × CH), 132.33 (2 × C), 130.09 (4 × C), 126.90 (2 × CH), 124.90 (4 × CH), 29.32 (4 × CH), 24.90 (4 × CH<sub>3</sub>), 23.90 (4 × CH<sub>3</sub>). Data consistent with literature.<sup>115</sup>

### 1,3-Bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate



1,3-Bis(2,6-diisopropylphenyl)imidazolium chloride (6.63 g, 15.6 mmol) was dissolved in the minimum amount of water. To this, tetrafluoroboric acid (48% wt. in H<sub>2</sub>O, 2.3 mL, 17.2 mmol) was added and a white precipitate was formed immediately. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 100 mL) and the combined organic layers dried over MgSO<sub>4</sub> before the solvent was removed *in vacuo* to give a crude amorphous off-white product. This was then re-dissolved in the minimum amount of CH<sub>2</sub>Cl<sub>2</sub> and Et<sub>2</sub>O (~200 mL) added to form a precipitate. This was then filtered and washed with Et<sub>2</sub>O (3 × 50 mL) to give the product as an amorphous white solid (5.5 g, 74%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.72 (1H, app t., *J* = 1.7 Hz, N(CH)N), 7.83 (2H, d, *J* = 1.6 Hz, NC=CH), 7.60 (2H, t, *J* = 7.9 Hz, ArH), 7.38 (4H, d, *J* = 7.8 Hz, ArH), 2.44 (4H, sept, *J* = 6.8 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.30 (12H, d, *J* = 6.8 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.23 (12H, d, *J* = 6.9 Hz, CH(CH<sub>3</sub>)<sub>2</sub>). <sup>13</sup>C NMR (125.8 MHz, CDCl<sub>3</sub>) δ 145.21 (CH), 137.81 (2 × CH), 132.47 (2 × C), 129.90 (4 × C), 126.79 (2 × CH), 124.98 (4 × CH), 29.31 (4 × CH), 24.67 (4 × CH<sub>3</sub>), 23.98 (4 × CH<sub>3</sub>). <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -152.67. Data consistent with literature.<sup>114</sup>

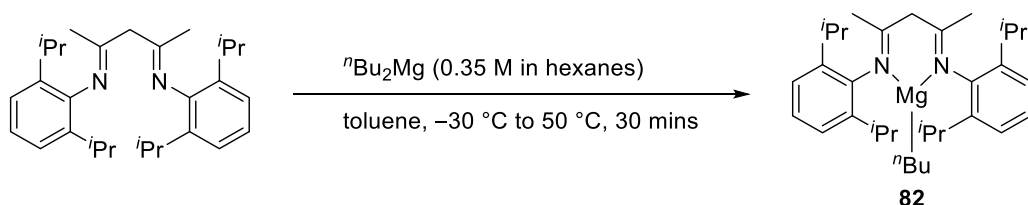
### 1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr)



In a glovebox, 1,3-bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate (5.5 g, 11.6 mmol) was suspended in THF (50 mL). To this, sodium hydride (0.56 g, 23.2 mmol) was added slowly and a spatula tip of potassium *tert*-butoxide (~ 0.1g) was added. The reaction vessel was closed with a septum and a vent needle inserted. The reaction mixture was then stirred overnight. The reaction mixture was then filtered and washed with THF (20 mL). The solvent was then removed and hexane was added to form an amorphous off-white precipitate. This was collected and dried under vacuum to give the product (0.96 g, 21 %). <sup>1</sup>H NMR  $\delta$  (500 MHz, C<sub>6</sub>D<sub>6</sub>) 7.32 – 7.28 (2H, m, ArH), 7.19 (4H, d,  $J$  = 7.7 Hz, ArH), 6.62 (2H, s, NC=CH), 2.97 (4H, sept,  $J$  = 6.9 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.29 (12H, d,  $J$  = 6.9 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.19 (12H, d,  $J$  = 7.0 Hz, CH(CH<sub>3</sub>)<sub>2</sub>). <sup>13</sup>C NMR (125.78 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  220.65 (C), 146.32 (CH), 139.01 (CH), 129.03 (2  $\times$  C), 128.35 (4  $\times$  C), 123.71 (2  $\times$  CH), 121.57 (4  $\times$  CH), 28.81 (4  $\times$  CH), 24.81 (4  $\times$  CH<sub>3</sub>), 23.64 (4  $\times$  CH<sub>3</sub>). Data consistent with literature.<sup>114</sup>

## Synthesis of Magnesium Complexes

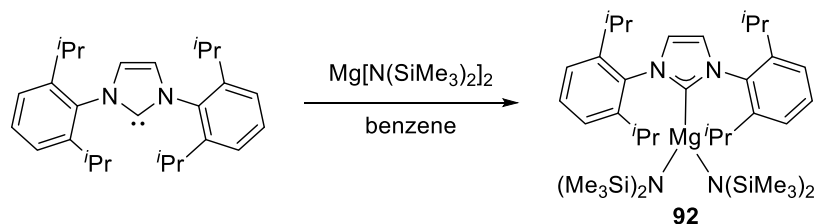
### Alkylmagnesium “nacnac” complex (82)



Prepared according to a procedure reported by Gibson.<sup>68b</sup>

“Nacnac” (0.42g, 1 mmol) was dissolved in toluene (15 mL) and then cooled to –30 °C. To this, a solution of dibutylmagnesium (0.35 M in hexanes, 2.85 mL, 1 mmol) was added slowly. The reaction mixture was then heated to 50 °C for 30 minutes. The solution was then used immediately in a reaction without isolation.

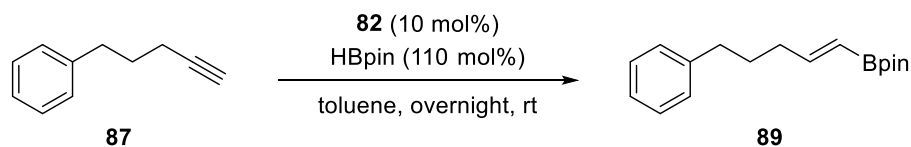
### IPrMg[N(SiMe<sub>3</sub>)<sub>2</sub>]<sub>2</sub> (**92**)



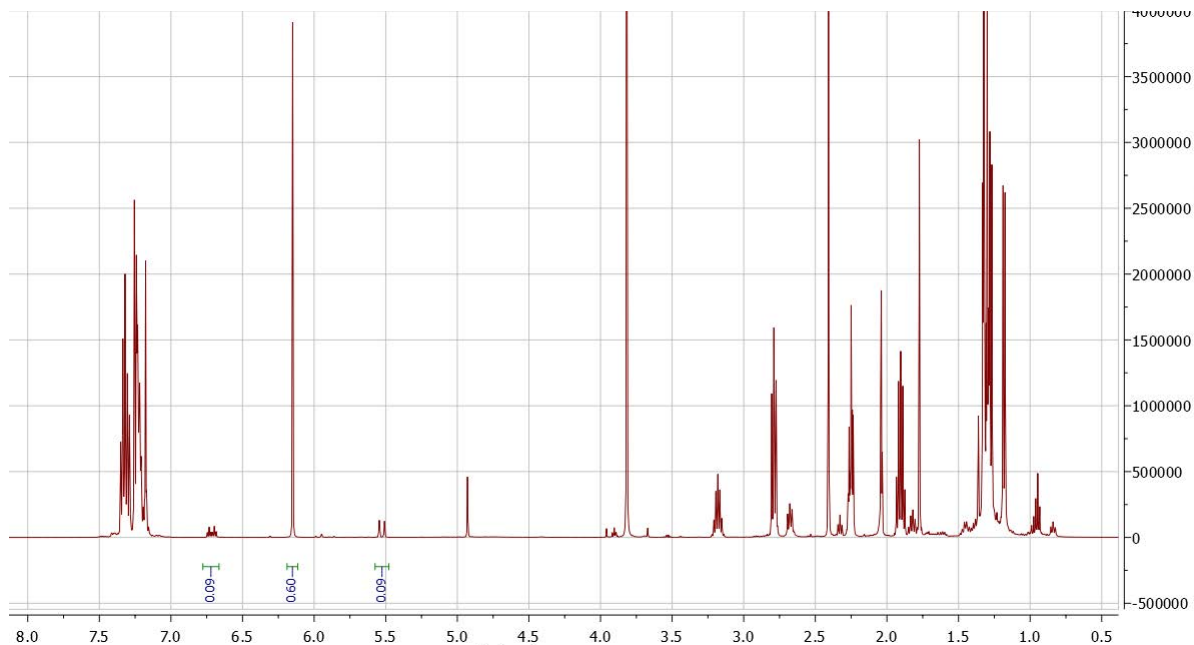
Magnesium bis(hexamethyldisilazide) (175 mg, 0.5 mmol) and IPr (195 mg, 0.5 mmol) were dissolved in benzene (15 mL). The reaction mixture was concentrated and cooled slowly to give the product as an amorphous solid (124 mg, 34%). <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ 7.12-7.26 (6H, m, ArH), 6.34 (2H, s, NC=CH), 2.83 (4H, sept, *J* = 6.81 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 1.43 (12H, d, *J* = 6.81 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 0.89 (12H, d, *J* = 6.81 Hz, CH(CH<sub>3</sub>)<sub>2</sub>), 0.20 (36H, s, Si(CH<sub>3</sub>)<sub>3</sub>). <sup>13</sup>C NMR (100.61 MHz, C<sub>6</sub>D<sub>6</sub>) δ 145.38, 130.59, 124.72, 28.43, 25.75, 23.07, 6.70. C<sup>1</sup> NHC carbon not observed. Data consistent with literature.<sup>86</sup>

### 6.4.3: Olefin Hydroboration Screenings (Table 8, p. 39)

#### Entry 6



General procedure F was applied to 5-phenyl-1-pentyne **87** (0.29 g, 2 mmol), **82** (3.6 mL, 0.2 mmol) and pinacol borane (0.3 mL, 2.05 mmol). The vinyl boronic ester product **89** was obtained in a 9% yield.



$^1\text{H}$  NMR Data (500 MHz,  $\text{CDCl}_3$ ):

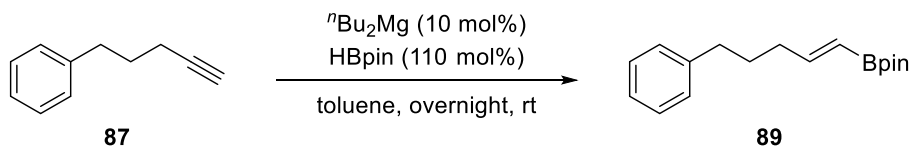
1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.15 (s, 3 H) ppm. Integral set to 0.6 (0.2/1  $\times$  3H = 0.6).

4,4,5,5-tetramethyl-2-[(1E)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane **89**: 6.72 (dt,  $J$  = 18.0, 6.4 Hz, 1 H, alkenyl CH), 5.53 (dt,  $J$  = 18.0, 1.6 Hz, 1 H, alkenyl CH) ppm. 9% yield of vinyl boronic ester product.

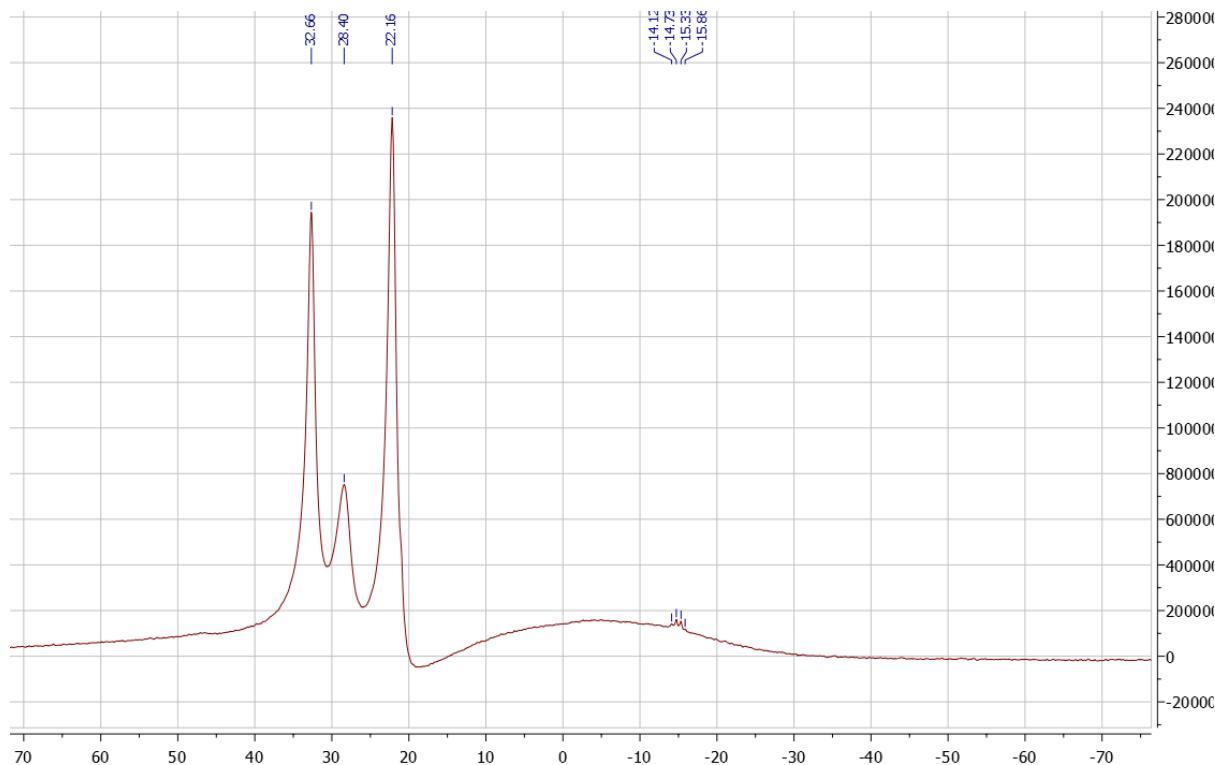
Data consistent with literature values.<sup>116</sup>

## 6.4.4: Further Reactions using 5-Phenyl-1-pentyne

### Control reaction without ligand



General procedure F was applied to 5-phenyl-1-pentyne **87** (0.14 g, 1 mmol),  $n\text{-Bu}_2\text{Mg}$  (0.29 mL, 0.1 mmol) and pinacol borane (0.15 mL, 1.05 mmol). The yield of vinyl boronic ester product **89** was determined to be 3% by  $^1\text{H}$  NMR spectroscopy. Analysis of  $^{11}\text{B}$  NMR spectra showed large amounts of  $n\text{-BuBpin}$  formation.



$^{11}\text{B}$  NMR Data (160 MHz,  $\text{CDCl}_3$ ):

4,4,5,5-tetramethyl-2-[(1E)-5-phenylpent-1-en-1-yl]-1,3,2-dioxaborolane **89**: 32.7 (s) ppm.

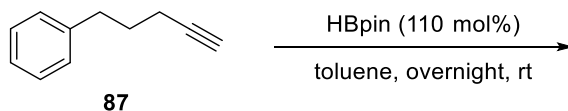
Pinacol borane: 28.4 (s) ppm

1-Butylboronic acid pinacol ester: 22.2 (s) ppm

Borane: -15.0 (q) ppm.

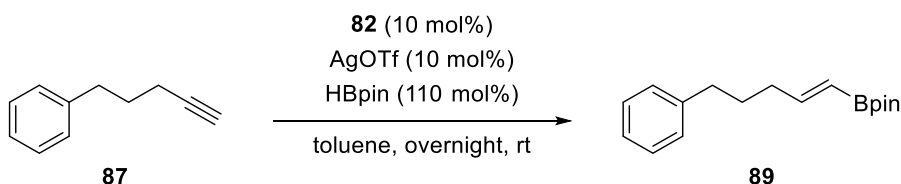
No literature data for  $^{11}\text{B}$  NMR of vinyl boronic ester or borane, so peaks are presumed. Other data consistent with literature values.<sup>116,117,118</sup>

### Control reaction without magnesium complex



General procedure F was applied to 5-phenyl-1-pentyne **87** (0.14 g, 1 mmol) and pinacol borane (0.15 mL, 1.05 mmol). No reaction occurred.

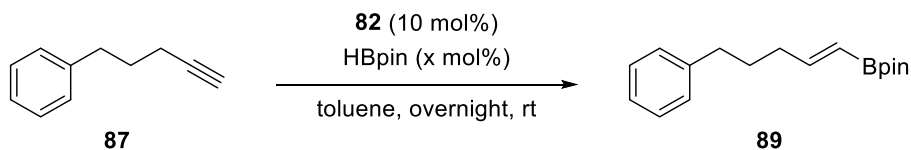
### Reaction with a $\pi$ -acid



General procedure F was applied to 5-phenyl-1-pentyne **87** (0.29 g, 2 mmol), **82** (3.6 mL, 0.2 mmol), silver triflate (51.4 mg, 0.2 mmol) and pinacol borane (0.3 mL). The yield of vinyl boronic ester product **89** was determined to be 4% by  $^1\text{H}$  NMR spectroscopy.

Data was consistent with literature values.<sup>116</sup>

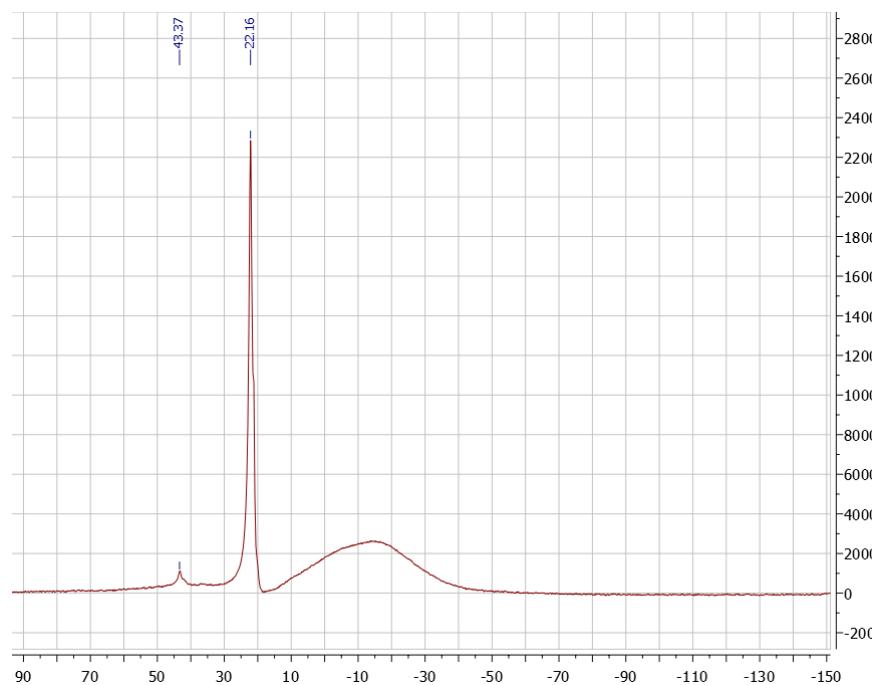
### Stoichiometric reactions



General procedure F was applied to 5-phenyl-1-pentyne **87** (57.7 mg, 0.4 mmol), **89** (7.14 mL, 0.4 mmol) and pinacol borane (1-3 equivalents).

1 equivalent of HBPin:

No vinyl boronic ester observed by  $^1\text{H}$  NMR, despite some consumption of starting material.

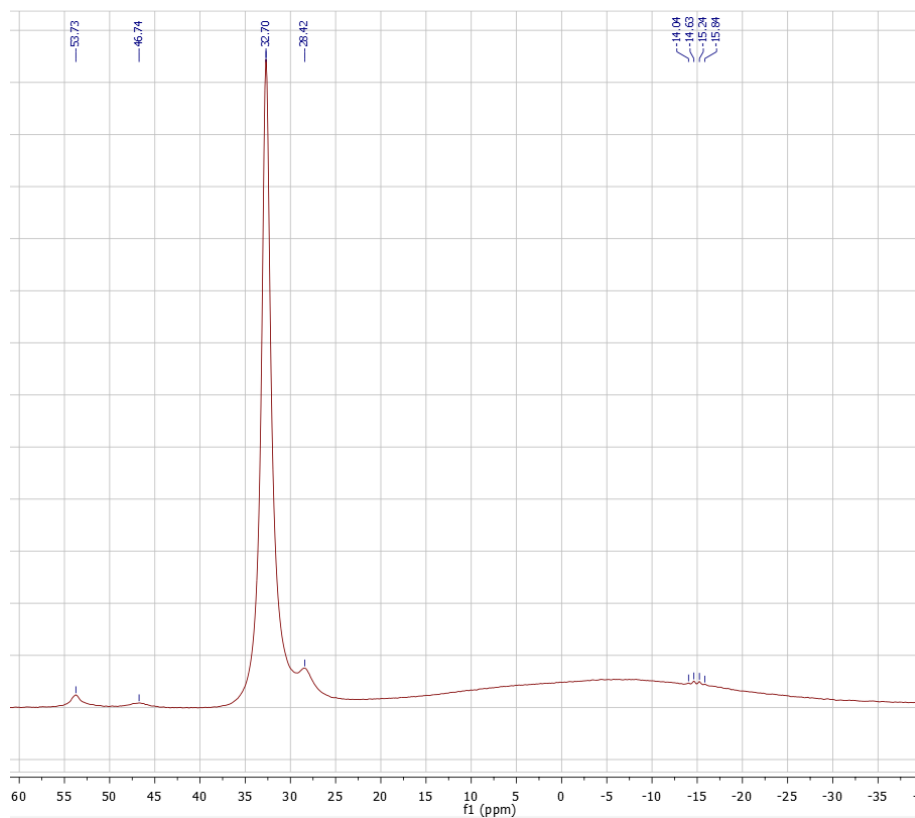


$^{11}\text{B}$  NMR (160 MHz,  $\text{CDCl}_3$ )  $\delta$  43.4 (potential tri-alkynyl species), 22.2 ( $n\text{BuBpin}$ ) ppm. Data compared with a previously reported tri-alkynyl species.<sup>119</sup>

2 equivalents of HBpin:

4% of the vinyl boronic ester **89** observed by  $^1\text{H}$  NMR. Data consistent with literature values.<sup>116</sup>

Two septet peaks present at 3.14 and 2.90 ppm from the isopropyl groups on the ligand.



$^{11}\text{B}$  NMR (160 MHz,  $\text{CDCl}_3$ )  $\delta$  32.7 (pinacol borane), 28.4 (vinyl boronic ester), -14.9 ( $\text{BH}_3$ ) ppm. Peak at 46.7 ppm could potentially be a tri-alkynyl species.<sup>119</sup>

3 equivalents of HBpin:

5% of the vinyl boronic ester **89** observed by  $^1\text{H}$  NMR. Data consistent with literature values.<sup>116</sup>

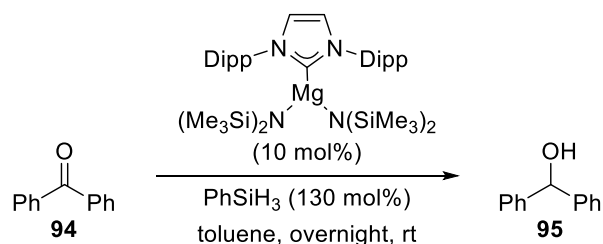
Two septet peaks present at 3.15 and 2.90 ppm from the isopropyl groups of the ligand.

The  $^{11}\text{B}$  NMR spectra showed a similar distribution of peaks with an addition peak at 21.0 ppm which could be assigned to the 1-butylboronic acid pinacol ester.

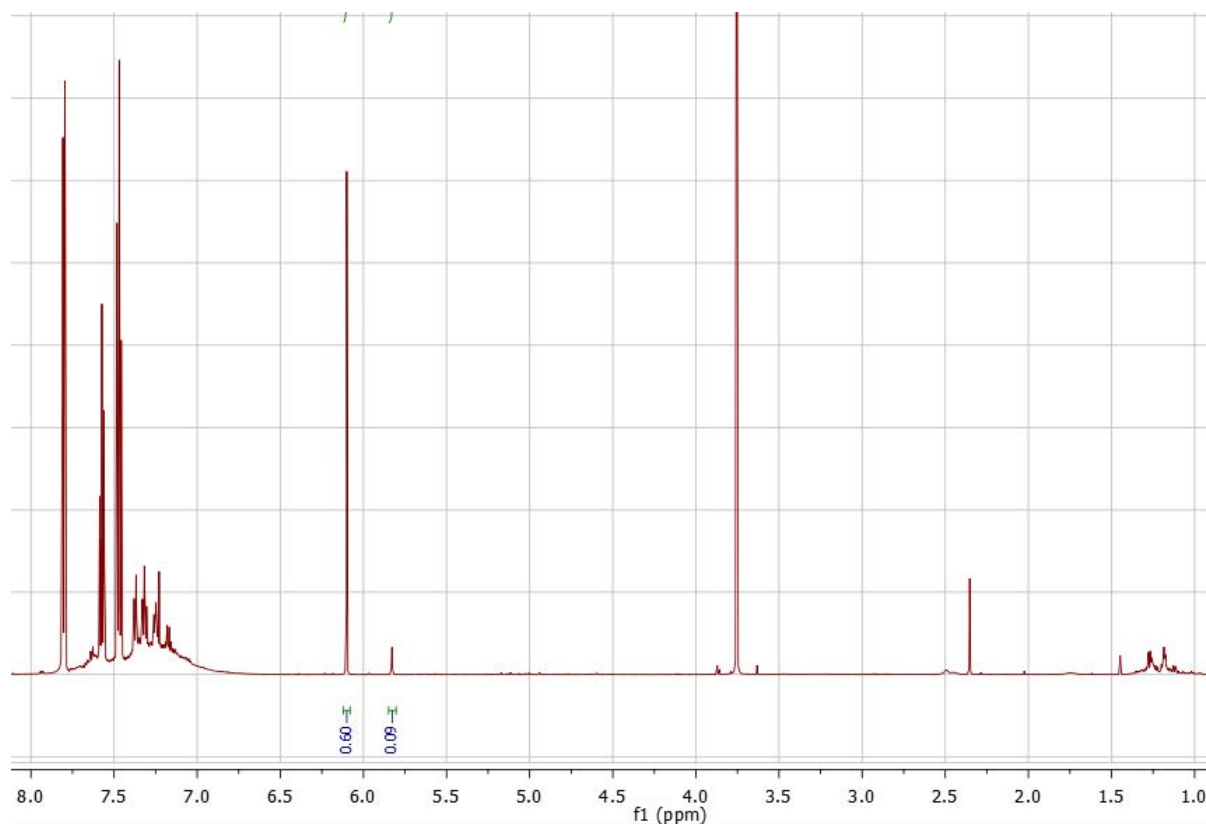


## 6.4.5: Ketone Reduction Screening Reactions (Table 9, p. 44)

### Entry 1



General procedure G was applied to benzophenone **94** (0.18 g, 1 mmol), **92** (78.5 mg, 0.1 mmol), phenylsilane (0.13 mL, 1.05 mmol) and toluene (1.25 mL). The yield of alcohol product **95** was determined to be 9%.



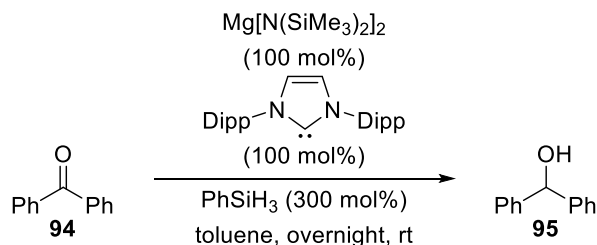
<sup>1</sup>H NMR Data (600 MHz, CDCl<sub>3</sub>):

1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.10 (s, 3 H) ppm. Integral set to 0.6 (0.2/1 × 3H = 0.6).

Diphenylmethanol **95**: 5.83 (s, 1 H, benzylic CH) ppm. Alcohol peak not seen due to concentration of sample. 9% yield of alcohol product **95**.

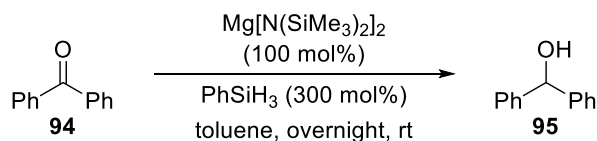
Data consistent with literature values.<sup>120</sup>

## Entry 2



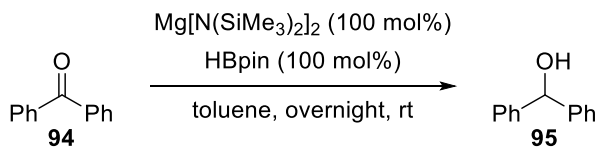
General procedure G was applied to benzophenone **94** (54.6 mg, 0.3 mmol),  $\text{Mg}[\text{N}(\text{SiMe}_3)_2]_2$  (103.5 mg, 0.3 mmol), IPr (116.6 mg, 0.3 mmol), phenylsilane (0.11 mL, 0.9 mmol) and toluene (0.5 mL). The yield of alcohol product **95** was determined to be 85%. Data consistent with literature values.<sup>120</sup>

## Entry 3



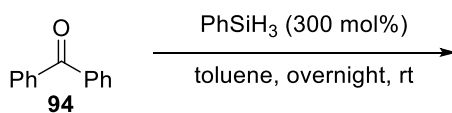
General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{Mg}[\text{N}(\text{SiMe}_3)_2]_2$  (173 mg, 0.5 mmol), phenylsilane (0.19 mL, 1.5 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 23%. Data was consistent with literature values.<sup>120</sup>

## Entry 4



General procedure G was applied to benzophenone **94** (91 mg, 0.5 mmol),  $\text{Mg}[\text{N}(\text{SiMe}_3)_2]_2$  (173 mg, 0.5 mmol), pinacol borane (74  $\mu\text{L}$ , 0.51 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 78%. Data was consistent with literature values.<sup>120</sup>

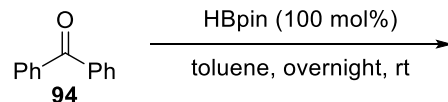
## Entry 5



General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol), phenylsilane (0.19 mL, 1.5

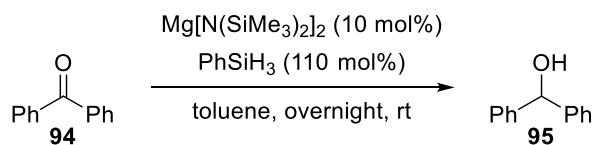
mmol) and toluene (2 mL). The reaction returned only starting material.

#### Entry 6



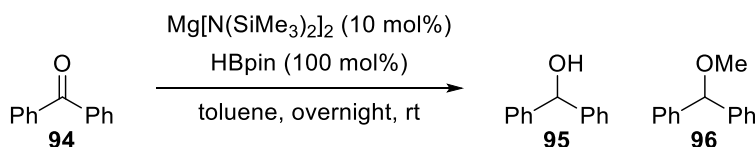
General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol), pinacol borane (74  $\mu$ L, 0.51 mmol) and toluene (2 mL). The reaction returned only starting material.

#### Entry 7

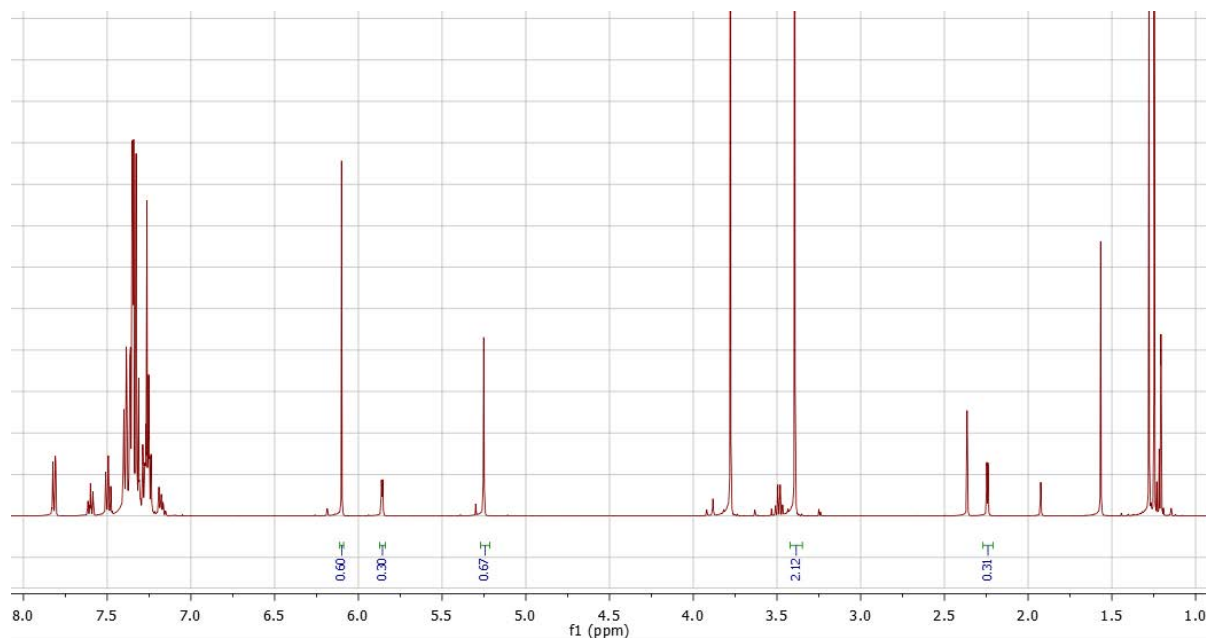


General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{Mg}[\text{N}(\text{SiMe}_3)_2]_2$  (17.3 mg, 0.05 mmol), phenylsilane (74  $\mu$ L, 0.6 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 12%. Data was consistent with literature values.<sup>120</sup>

#### Entry 8



General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{Mg}[\text{N}(\text{SiMe}_3)_2]_2$  (17.3 mg, 0.05 mmol), pinacol borane (74  $\mu$ L, 0.51 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 30% and the yield of methyl ether product **96** was determined to be 67%.



<sup>1</sup>H NMR Data (500 MHz, CDCl<sub>3</sub>):

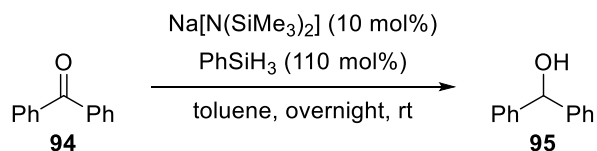
1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.10 (s, 3 H) ppm. Integral set to 0.6 (0.2/1 × 3H = 0.6).

Diphenylmethanol **95**: 5.86 (d, *J* = 3.4 Hz, 1 H, benzylic CH), 2.24 (d, *J* = 3.6 Hz, 1 H, OH) ppm. 30% of the alcohol product.

(Methoxymethylene)dibenzene **96**: 5.25 (s, 1 H, benzylic CH), 3.39 (s, 3 H, OCH<sub>3</sub>) ppm. 67% of the ether product.

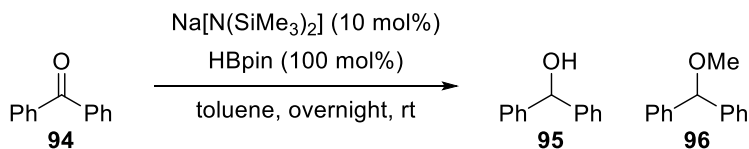
Data were consistent with literature values.<sup>120,121</sup>

## Entry 9



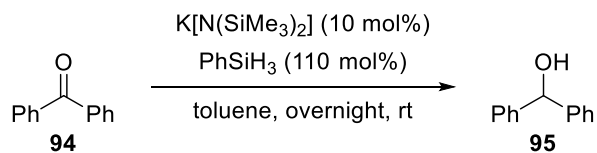
General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol), Na[N(SiMe<sub>3</sub>)<sub>2</sub>] (9.17 mg, 0.05 mmol), phenylsilane (74 μL, 0.6 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 20%. Data was consistent with literature values.<sup>120</sup>

### Entry 10



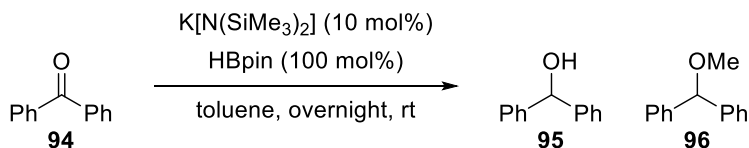
General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{Na}[\text{N}(\text{SiMe}_3)_2]$  (9.17 mg, 0.05 mmol), pinacol borane (74  $\mu\text{L}$ , 0.51 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 29% and the yield of methyl ether product **96** was determined to be 63%. Data was consistent with literature values.<sup>120,121</sup>

### Entry 11



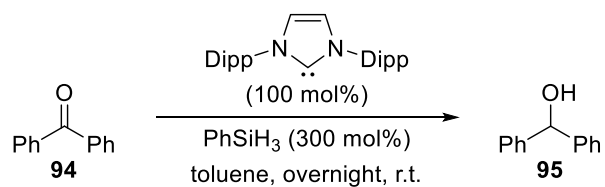
General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{K}[\text{N}(\text{SiMe}_3)_2]$  (9.97 mg, 0.05 mmol), phenylsilane (74  $\mu\text{L}$ , 0.6 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 14%. Data was consistent with literature values.<sup>120</sup>

### Entry 12



General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol),  $\text{K}[\text{N}(\text{SiMe}_3)_2]$  (9.97 mg, 0.05 mmol), pinacol borane (74  $\mu\text{L}$ , 0.51 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 17% and the yield of methyl ether product **96** was determined to be 70%. Data was consistent with literature values.<sup>120,121</sup>

### Entry 13

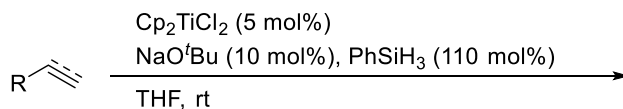


General procedure G was applied to benzophenone **94** (91.1 mg, 0.5 mmol), IPr (194 mg, 0.5 mmol), phenylsilane (0.19 mL, 1.5 mmol) and toluene (2 mL). The yield of alcohol product **95** was determined to be 80%. Data was consistent with literature values.<sup>120</sup>

## 6.5: Titanium-Catalysed Hydrogenation and Hydrosilylation of Olefins

### 6.5.1: General Procedures

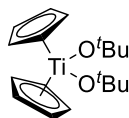
#### General Procedure H: Titanium-Catalysed Hydrosilylation of Olefins



In a glovebox, titanocene dichloride (8.7 mg, 0.035 mmol) and sodium *tert*-butoxide (6.7 mg, 0.07 mmol) were weighed into a carousel tube equipped with a stirrer bar. After sealing the tubes and removing from the glovebox, phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) was added directed to the mixture, followed by 4-*tert*-butylstyrene (0.13 mL, 0.7 mmol) and the reaction mixture diluted with THF (2 mL). After stirring at room temperature, the reactions were diluted with Et<sub>2</sub>O (10 mL) and 1,3,5-trimethoxybenzene (23.5 mg) added to the solution. An aliquot sample was taken and the solvent removed *in vacuo*. Known products were identified by <sup>1</sup>H NMR spectroscopy and characterised by comparison to authentic samples of spectral data.

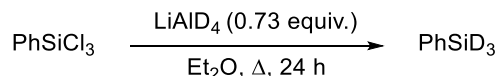
## 6.5.2: Synthesis of Complexes and Reagents

### Titanocene bis-*tert*-butoxide



In a glovebox, titanocene dichloride (1.25 g, 5 mmol) and lithium *tert*-butoxide (0.81 g, 10 mmol) were dissolved in anhydrous THF (10 mL) and the reaction mixture was stirred for 24 hours. The solvent was then removed *in vacuo* and the resulting oil was extracted into hexanes. The extracts were then filtered through a frit under inert gas and the solvent removed *in vacuo* to give a yellow-orange oil as the crude product.  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  6.00 (10 H, s,  $\text{C}_5\text{H}_5$ ), 1.18 (18 H, s,  $\text{OC}(\text{CH}_3)_3$ ). Data consistent with literature values.<sup>122</sup>

### $\text{d}_3$ -Phenylsilane

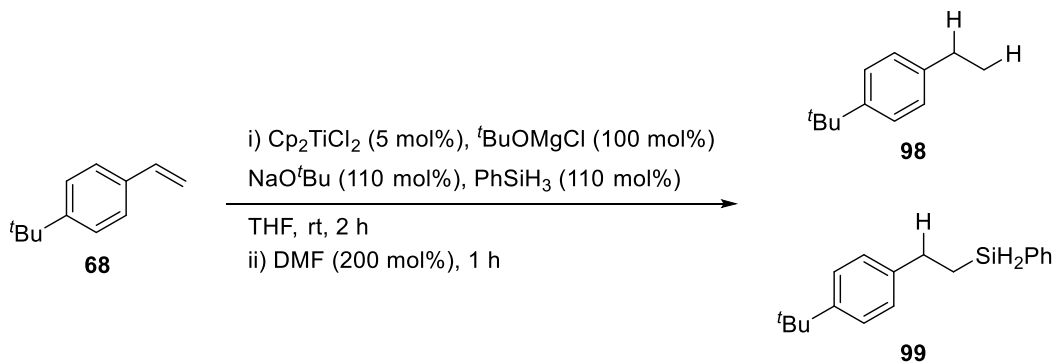


To a stirred suspension of lithium aluminium deuteride (1 g, 23.8 mmol) in diethyl ether (30 mL), trichloro(phenyl)silane (5.2 mL, 32.6 mmol) was added dropwise. The reaction was then heated at reflux for 24 hours. After removing from the heat, the reaction mixture was diluted with diethyl ether (30 mL) and cooled to 0 °C. Once cooled, water (1 mL) was very slowly added to the reaction followed by sodium hydroxide (15% aq. soln., 1 mL). Water (3 mL) was then added slowly and the reaction mixture was warmed to room temperature and stirred for 15 minutes. Anhydrous magnesium sulphate was then added and the mixture stirred for a further 15 minutes. The salts were then removed by filtration and the solvent carefully removed *in vacuo* to give the product as a colourless oil (1.07g, 30%). Analysis by  $^1\text{H}$  and  $^2\text{D}$  NMR spectroscopy showed complete deuterium incorporation.

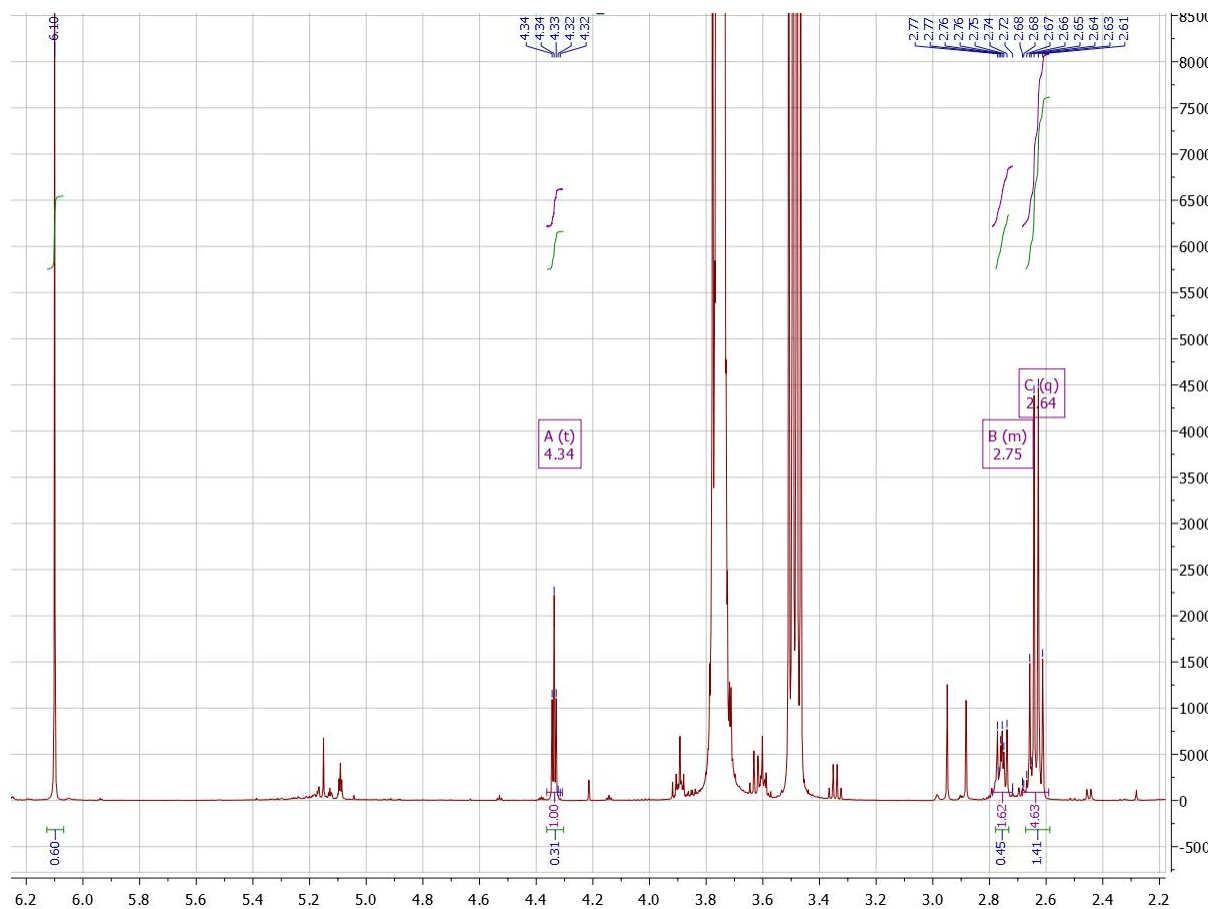


### 6.5.3: Initial Catalyst and Substrate Screen

#### Attempting hydromagnesiation in the absence of Grignard reagent



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), *tert*-butoxymagnesium chloride (93 mg, 0.7 mmol), sodium *tert*-butoxide (74 mg, 0.77 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). After stirring for 1 h, *N,N*-dimethylformamide (0.11 mL, 1.4 mmol) was added and the reaction was stirred for a further 1 h. Products were identified and yields determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. The hydrogenation product **98** was found in a 71% yield and the hydrosilylation product **99** was found in a 15% yield.



<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) Data:

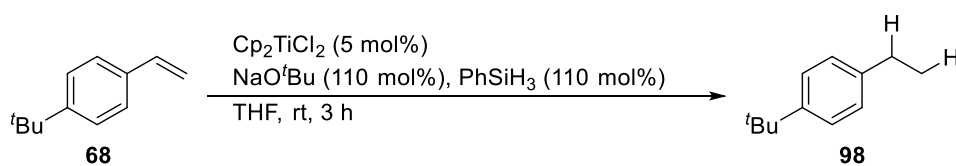
1,3,5-Trimethoxybenzene (20 mol%) used as internal standard: 6.10 (s, 3 H) ppm. Integral set to 0.6 (0.2/1 × 3H = 0.6).

**94** (H-H) 2.64 (q, *J* = 7.6 Hz, 2 H, ArCH<sub>2</sub>H<sub>3</sub>) ppm. 71% of hydrogenation product. Data consistent with literature values.<sup>123</sup>

**95** (H-Si) <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 4.34 (t, *J* = 3.6 Hz, 2 H, ArCH<sub>2</sub>CH<sub>2</sub>SiH<sub>2</sub>Ph), 2.75 (m, 2 H, ArCH<sub>2</sub>CH<sub>2</sub>SiH<sub>2</sub>Ph) ppm. 15% of hydrosilylation product (based off SiH<sub>2</sub> protons). Data consistent with literature values.<sup>34</sup>

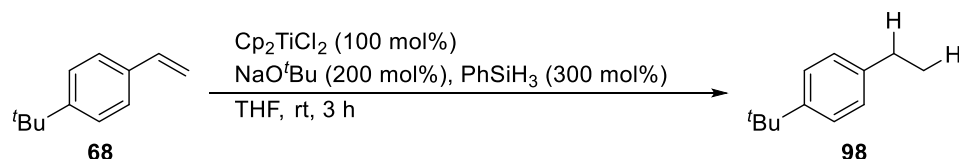
## Assessing Titanium-Catalysed Hydrosilylation (Table 10, p. 51)

### Entry 1



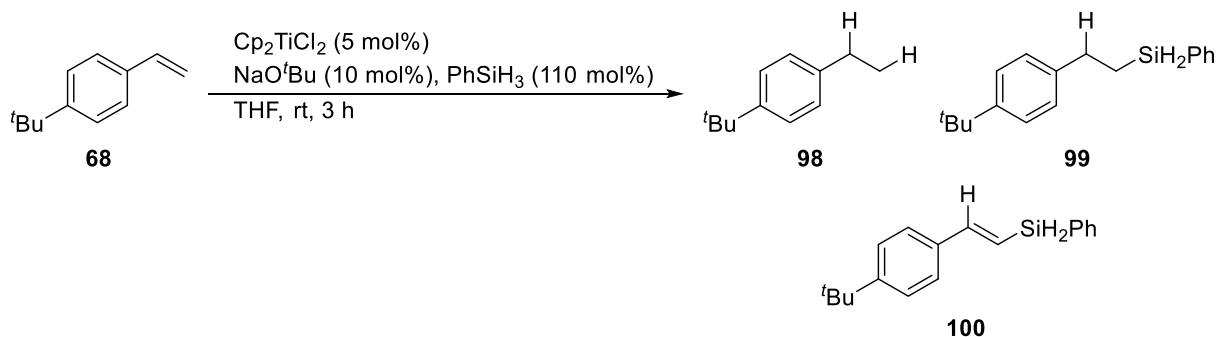
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (74 mg, 0.77 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. The hydrogenation product **98** was found to be the major product by  $^1\text{H}$  NMR with only trace amounts of the hydrosilylation product **99** observed in the  $^1\text{H}$  NMR spectra. The yield was determined to be 50% by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>123</sup>

### Entry 2



General procedure H was applied to titanocene dichloride (174 mg, 0.7 mmol), sodium *tert*-butoxide (135 mg, 1.4 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.26 mL, 2.1 mL) and THF (6 mL). The reaction was stirred for 3 h. The hydrogenation product **98** was observed in a 62% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene. Data was consistent with literature values.<sup>123</sup>

### Entry 3

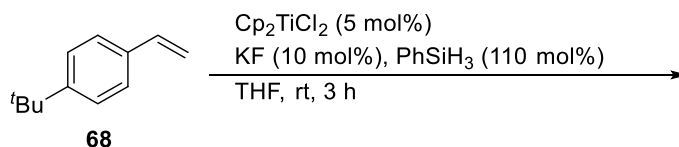


General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. Products were identified and yields determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. The hydrogenation product **98** was found in a 42% yield and the hydrosilylation product **99** was found in a 35% yield. Data were consistent with literature values.<sup>34,123</sup>

The presumed dehydrogenative silylation product **100** was also found in a 17% yield.

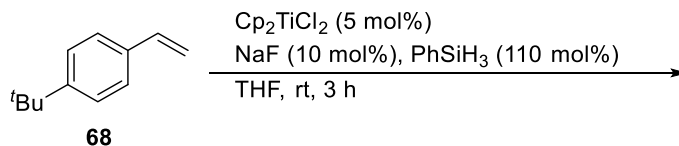
**95** (dehydrog. Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.52 (dt,  $J = 19.0, 3.3$  Hz, 1 H,  $\text{ArCH}=\text{CHSiH}_2\text{Ph}$ ), 4.75 (d,  $J = 3.3$  Hz, 2 H,  $\text{ArCH}=\text{CHSiH}_2\text{Ph}$ ) ppm.

#### Entry 4



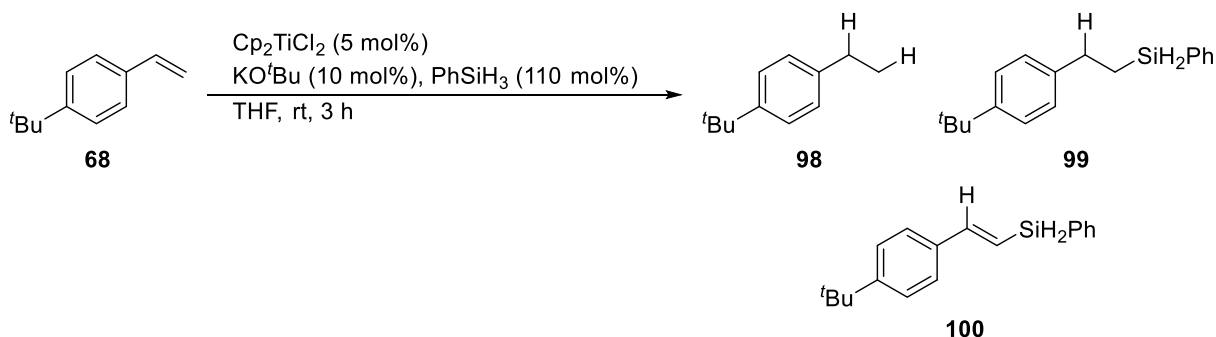
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), potassium fluoride (4.1 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. No reaction took place.

#### Entry 5



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium fluoride (2.9 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. No reaction took place.

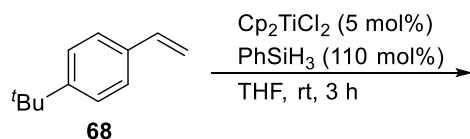
#### Entry 6



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), potassium *tert*-butoxide (7.9 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 3 h. The hydrogenation product **98** was observed in a 41% yield,

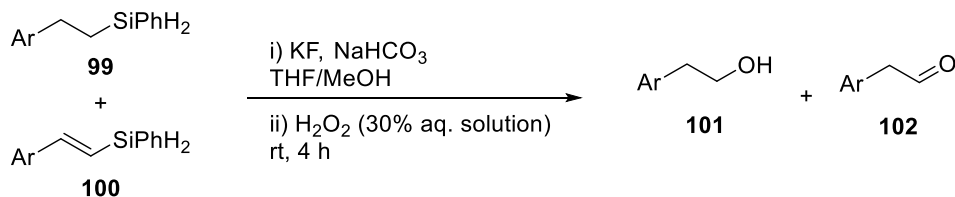
the hydrosilylation product **99** in a 40% yield and the dehydrogenative silylation product **100** in a 13% yield. Data were consistent with literature values.<sup>34,123</sup>

### Entry 7

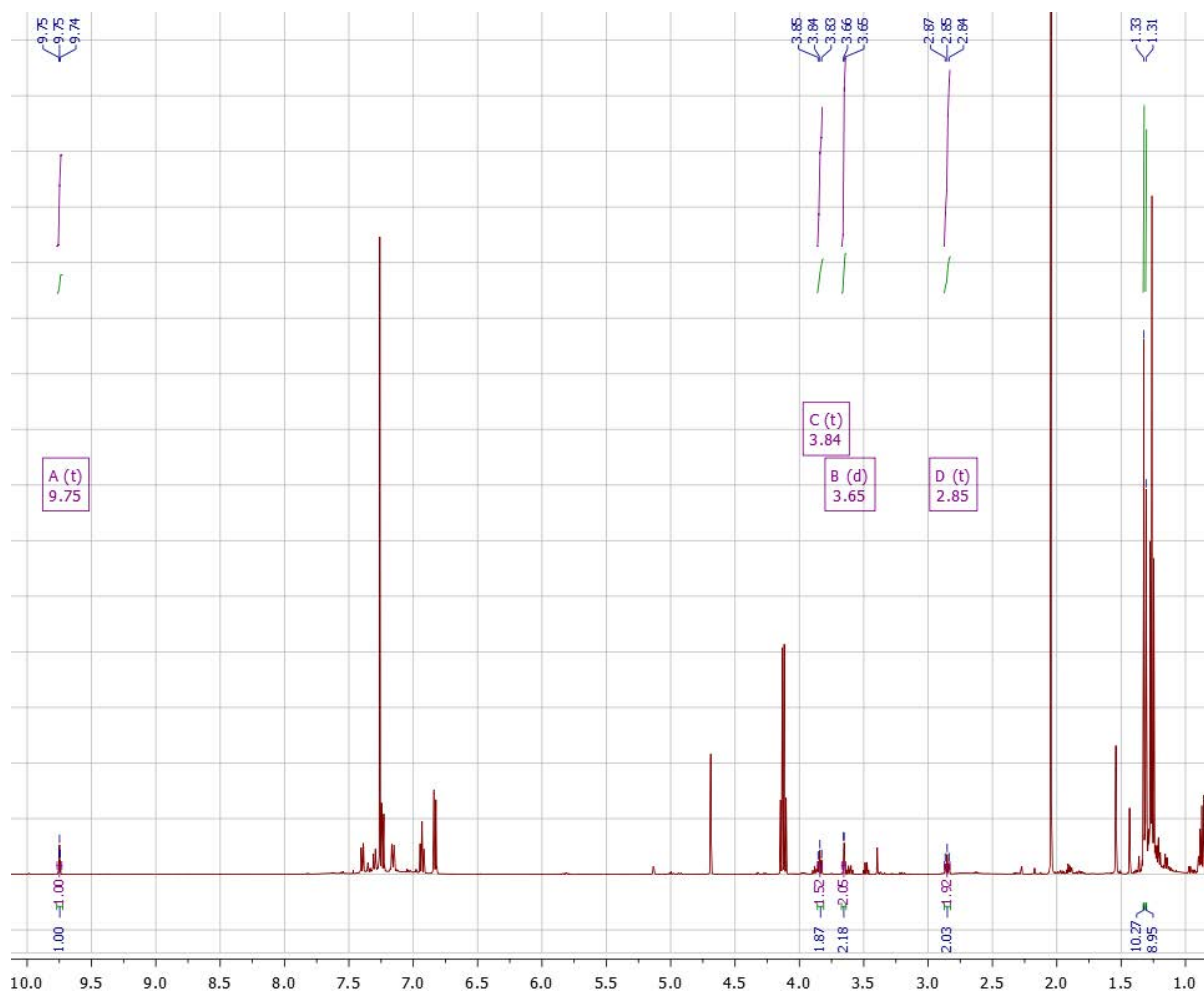


General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. No reaction took place.

### Oxidising reaction mixture to confirm dehydrogenative silylation



A crude reaction mixture of products **99** and **100** was dissolved in a mixture of THF (2 mL) and methanol (2 mL). To this, potassium fluoride (116.2 mg, 2 mmol) and sodium bicarbonate (92.4 mg, 1.1 mmol) were added and the mixture was stirred. While stirring, hydrogen peroxide (30% aqueous solution, 3 mL, 1 mmol) was added in one portion and the reaction left to stir for 4 hours. The reaction was then quenched with a saturated aqueous solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (20 mL) and the mixture extracted with ethyl acetate (20 mL), dried over  $\text{MgSO}_4$  and the solvents removed *in vacuo* to give an inseparable mixture of alcohol **101** and aldehyde **102**.



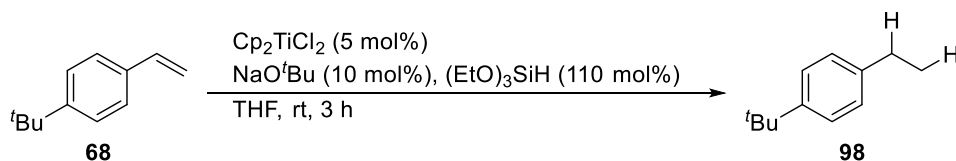
2-(4-(*tert*-Butyl)phenyl)ethan-1-ol **97**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  3.84 (t,  $J = 6.8$  Hz, 2 H,  $\text{ArCH}_2\text{CH}_2\text{OH}$ ), 2.85 (t,  $J = 7.4$  Hz, 2 H,  $\text{ArCH}_2\text{H}_2\text{OH}$ ) ppm.

4-*tert*-Butylphenylacetaldehyde **98**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.75 (t,  $J = 2.5$  Hz, 1 H,  $\text{ArCH}_2\text{CHO}$ ), 3.65 (d,  $J = 2.5$  Hz, 2 H,  $\text{ArCH}_2\text{CHO}$ ) ppm.

Data were consistent with literature values.<sup>124,125</sup>

## Olefin and Silane Screening (Table 11, p. 53)

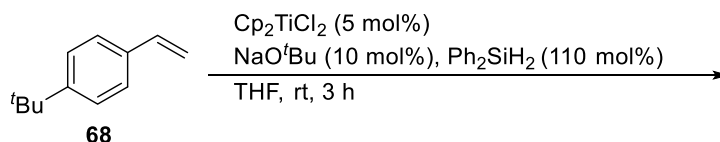
### Entry 1



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7

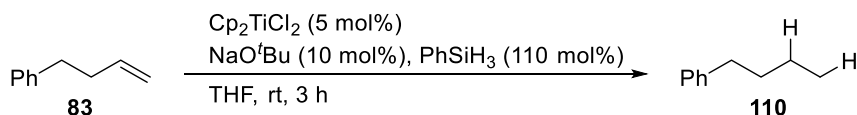
mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), triethoxysilane (0.14 mL, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. The hydrogenation product **98** was observed in a 55% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>123</sup>

### Entry 2



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), diphenylsilane (0.14 mL, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. No reaction took place.

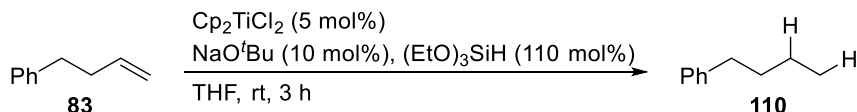
### Entry 3



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-phenyl-1-butene **83** (0.11 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. The hydrogenation product **110** was observed in a 25% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.69 – 2.65 (m, 2 H,  $\text{ArCH}_2$ ), 1.70 – 1.63 (m, 2 H,  $\text{ArCH}_2\text{CH}_2$ ), 1.00 – 0.97 (m, 3 H,  $\text{ArCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ). Data was consistent with literature values.<sup>123</sup>

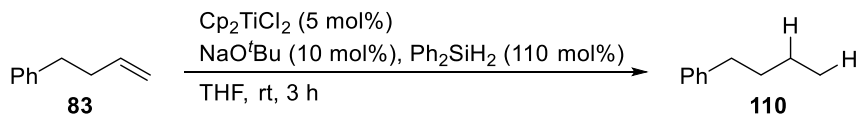
### Entry 4



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-phenyl-1-butene **83** (0.11 mL, 0.7 mmol), triethoxysilane (0.14  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. The hydrogenation product **110** was observed in a 10% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with

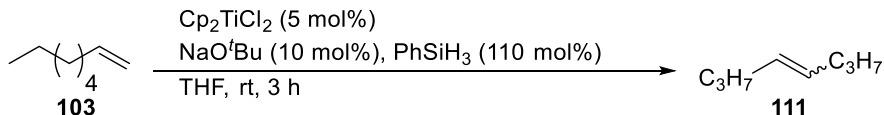
literature values.<sup>123</sup>

### Entry 5



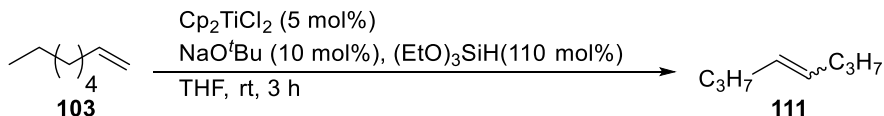
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-phenyl-1-butene **83** (0.11 mL, 0.7 mmol), diphenylsilane (0.14 mL, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. The hydrogenation product **110** was observed in a 4% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>123</sup>

### Entry 6



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), oct-1-ene **103** (0.11 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. Oct-4-ene **111** was observed as the product in a 16% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.45 – 5.38 (m, 2 H,  $\text{CH}=\text{CH}$ ). Data was consistent with literature values.<sup>126</sup>

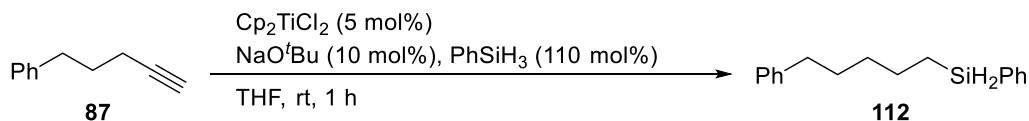
### Entry 7



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), oct-1-ene **103** (0.11 mL, 0.7 mmol), triethoxysilane (0.14 mL, 0.77 mmol) and THF (5 mL). The reaction was stirred for 3 h. Oct-4-ene **111** was observed as the product in a 19% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.43 – 5.31 (m, 2 H,  $\text{CH}=\text{CH}$ ). Data was consistent with literature values.<sup>126</sup>

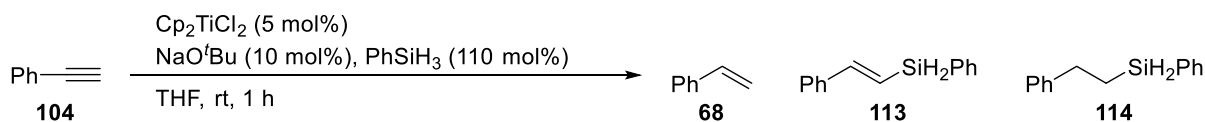


## Entry 8



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 5-phenyl-1-pentyne **87** (101 mg, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The reduced hydrosilylation product **112** was observed in an 18% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57 – 7.55 (m, 2 H, ArH), 7.40 – 7.27 (m, 5 H, ArH), 7.19 – 7.16 (m, 3 H, ArH), 4.28 (t,  $J = 3.7$  Hz, 2 H,  $\text{SiH}_2\text{Ph}$ ), 2.59 (t,  $J = 2.7$  Hz, 2 H, ArCH<sub>2</sub>), 1.62 (p,  $J = 7.7$  Hz, 2 H, CH<sub>2</sub>), 1.53 – 1.46 (m, 2 H, CH<sub>2</sub>), 1.45 – 1.38 (m, 2 H, CH<sub>2</sub>); HRMS (ESI) Exact mass calcd for  $\text{C}_{17}\text{H}_{22}\text{NaSi}$   $[\text{M}+\text{Na}]^+$ : 277.13970, found: 277.13940.

## Entry 9



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), phenylacetylene **104** (77  $\mu\text{L}$ , 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The hydrogenation product **68** was observed in a 5% yield, the hydrosilylation product **113** was observed in a 15% yield and the reduced hydrosilylation product **114** was observed in a 3% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

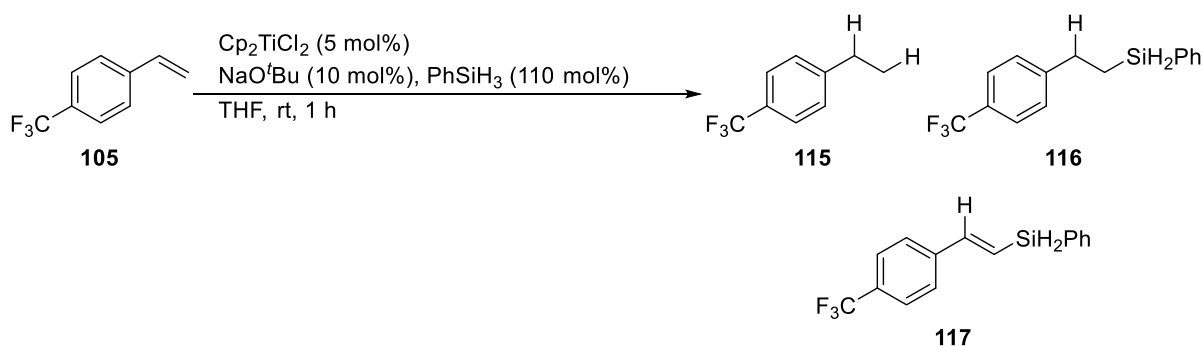
**68** (H-H)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.75 – 6.67 (m, 1 H,  $\text{PhCH}=\text{CH}_2$ ), 5.74 (dd,  $J = 17.6, 0.9$  Hz, 1 H,  $\text{PhCH}=\text{CH}_2$ ), 5.23 (dd,  $J = 10.9, 0.9$  Hz, 1 H,  $\text{PhCH}=\text{CH}_2$ ).

**113** (H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.50 (dt,  $J = 19.0, 3.3$  Hz, 1 H,  $\text{PhCH}=\text{CHSiH}_2\text{Ph}$ ).

**114** (reduc. H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.31 (t,  $J = 3.6$  Hz, 2 H,  $-\text{SiH}_2\text{Ph}$ ), 2.79 – 2.73 (m, 2 H,  $\text{PhCH}_2\text{CH}_2\text{SiH}_2\text{Ph}$ ).

Data were consistent with literature values.<sup>33,127</sup>

## Entry 10



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-trifluoromethylstyrene **105** (0.1 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The hydrogenation product **115** was observed in a 42% yield, the hydrosilylation product **116** was observed in a 32% yield and the dehydrogenative silylation product **117** was observed in a 22% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Hydrosilylation product and dehydrogenative hydrosilylation product were identified by comparison to  $^1\text{H}$  NMR data for **99** and **100**.

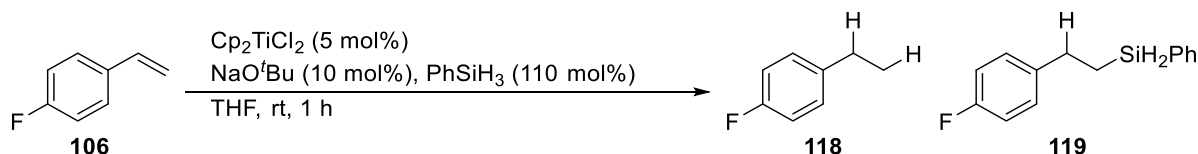
**115** (H-H)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.63 (q,  $J = 7.6$  Hz, 2 H,  $\text{ArCH}_2\text{H}_3$ ), 1.25 (t,  $J = 7.6$  Hz, 3 H,  $\text{ArCH}_2\text{H}_3$ ).

**116** (H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.33 (t,  $J = 3.6$  Hz, 2 H,  $-\text{SiH}_2\text{Ph}$ ), 2.79-2.72 (m, 2 H,  $\text{ArCH}_2\text{H}_2\text{SiH}_2\text{Ph}$ ).

**117** (dehydrog. Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.47 (dt,  $J = 19.0, 3.3$  Hz, 1 H,  $\text{ArCH}=\text{CHSiH}_2\text{Ph}$ ).

Data were consistent with literature values.<sup>128</sup>

## Entry 11



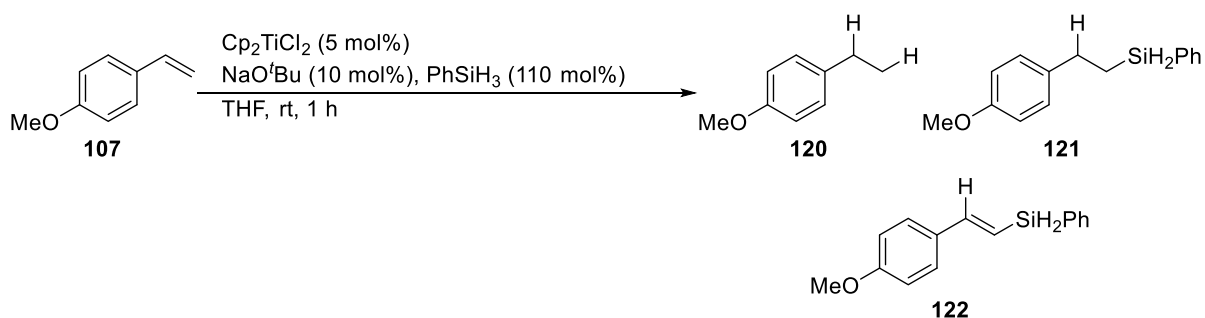
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-fluorostyrene **106** (83  $\mu\text{L}$ , 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The hydrogenation product **118** was observed in a 37% yield and the hydrosilylation product **119** was observed in a 43% yield. The yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

**118** (H-H)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.60 (q,  $J = 7.6$  Hz, 2 H,  $\text{ArCH}_2\text{CH}_3$ ).

**119** (H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.28 (t,  $J = 3.6$  Hz, 2 H,  $-\text{SiCH}_2\text{Ph}$ ), 2.76 – 2.69 (m, 2 H,  $\text{ArCH}_2\text{CH}_2\text{SiH}_2\text{Ph}$ ).

Data were consistent with literature values.<sup>35,129</sup>

### Entry 12



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-methoxystyrene **107** (93  $\mu\text{L}$ , 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The hydrogenation product **120** was observed in a 43% yield, the hydrosilylation product **121** was observed in a 30% yield and the dehydrogenative silylation product **122** was observed in a 15% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Dehydrogenative silylation product was identified by comparison to NMR data for **100**.

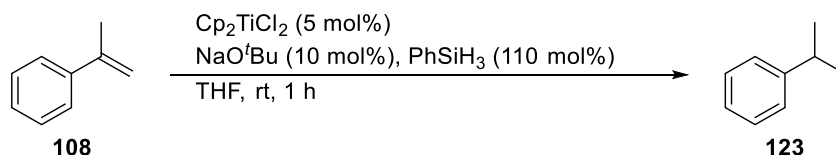
**120** (H-H)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.57 (q,  $J = 7.6$  Hz, 2 H,  $\text{ArCH}_2\text{H}_3$ ).

**121** (H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.28 (t,  $J = 3.6$  Hz, 2 H,  $-\text{SiH}_2\text{Ph}$ ), 2.73-2.66 (m, 2 H,  $\text{ArCH}_2\text{SiH}_2\text{Ph}$ ).

**122** (dehydrog. H-Si)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.31 (dt,  $J = 18.9, 3.3$  Hz, 1 H,  $\text{ArCH}=\text{CHSiH}_2\text{Ph}$ ).

Data were consistent with literature values.<sup>35,130</sup>

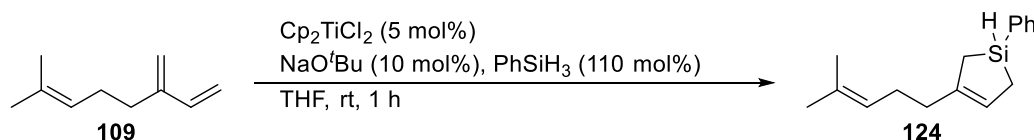
### Entry 13



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol),  $\alpha$ -methylstyrene **108** (91  $\mu\text{L}$ , 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The reaction was stirred for 1 h. The hydrogenation product **123** was observed in an 8% yield. The

yield was determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.93 (sept,  $J = 7.1$  Hz, 1 H,  $\text{CH}(\text{CH}_3)_2$ ), 1.28 (d,  $J = 6.9$  Hz, 6 H,  $\text{CH}(\text{CH}_3)_2$ ). Data were consistent with literature values.<sup>131</sup>

#### Entry 14



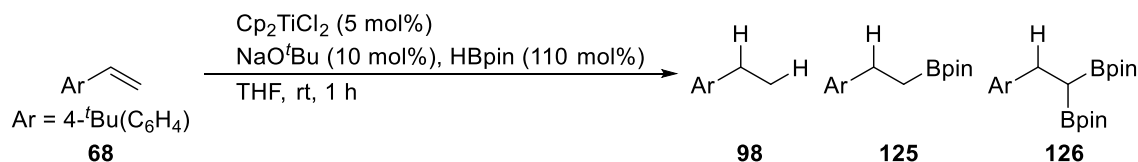
General procedure was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), myrcene **109** (120  $\mu\text{L}$ , 0.7 mmol), phenylsilane (0.17 mL, 1.4 mmol) and THF (2 mL). The reaction was stirred for 1 h. The major product was presumed to be the cyclic dehydrogenative silylation product **124**, obtained in a 48% yield.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.64 (m, 1 H,  $=\text{CH}$ ), 4.74 (tt,  $J = 3.1, 1.8$  Hz, 1 H,  $\text{SiHPh}$ ), 2.16 (app. s, 4 H,  $\text{CH}_2$ ).

Approximately 9% of another product, presumed to be either the 1,4-hydrosilylation or 1,2-hydrosilylation product, was also observed.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.32 (t,  $J = 3.9$  Hz, 2 H,  $-\text{SiH}_2\text{Ph}$ ).

Data were consistent with literature values.<sup>96</sup>

#### Hydroboration reaction with $\text{Cp}_2\text{TiCl}_2$



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), pinacol borane (112  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 20% yield, the linear hydroboration product **125** was observed in a 45% yield and the presumed geminal diboration product **126** was observed in a 22% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

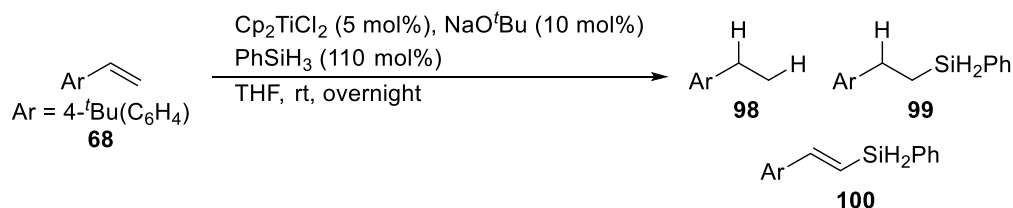
**125** (H-B)  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.70 (t,  $J = 8.2$  Hz, 2 H,  $\text{ArCH}_2\text{CH}_2\text{Bpin}$ ).

**126** (gem.  $2 \times \text{B}$ )  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  2.83 (d,  $J = 8.4$  Hz, 2 H,  $\text{ArCH}_2\text{CH}(\text{Bpin})_2$ ).

Data were consistent with literature values.<sup>123,132</sup>

## 6.5.4: Further Screening Reactions

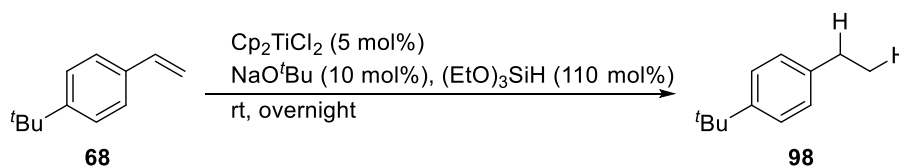
### Reaction concentration screening (Table 12, p. 55)



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (0.5 – 5 mL). Reactions were stirred overnight rather than for 3 hours.

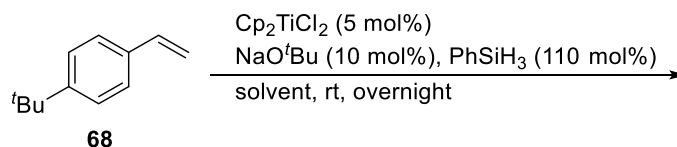
Yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

### Reaction with triethoxysilane in the absence of solvent



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol) and triethoxysilane (0.14 mL, 0.77 mmol). The hydrogenation product **98** was observed in a 60% yield. Data were consistent with literature values.<sup>123</sup>

### Solvent Screen



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and solvent (2 mL). The solvents used were as follows:

Diethyl ether – no reaction

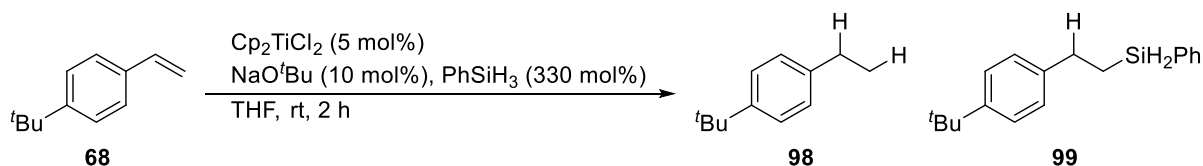
Dichloromethane – no reaction

Toluene – no reaction

Ethyl acetate – 14% hydrogenation product **98**.

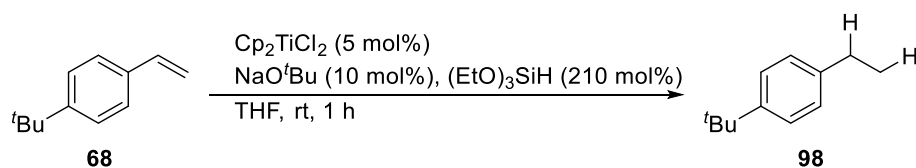
Data was consistent with literature values.<sup>123</sup>

### Reaction with excess phenylsilane



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.29 mL, 2.31 mmol) and THF (2 mL). The yield of hydrogenation product **98** was observed in 50% yield and the yield of hydrosilylation product **99** was observed in 50% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>34,123</sup>

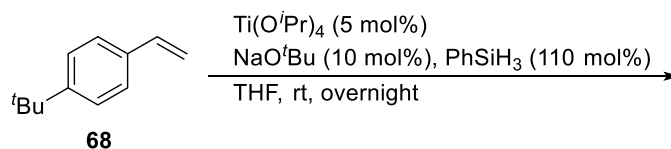
### Reaction with excess triethoxysilane



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), triethoxysilane (0.27 mL, 1.47 mmol) and THF (2 mL). The yield of hydrogenation product **98** was observed in a 60% yield by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>123</sup>

### Screening other commercially-available titanium pre-catalysts

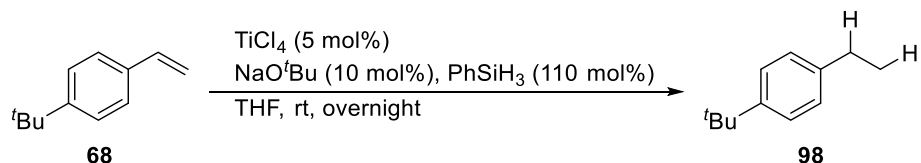
#### $\text{Ti}(\text{O}^i\text{Pr})_4$



General procedure H was applied to titanium(IV) *iso*-propoxide (10  $\mu\text{L}$ , 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77

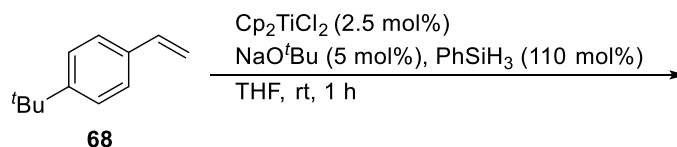
mmol) and THF (2 mL). No reaction took place.

### TiCl<sub>4</sub>



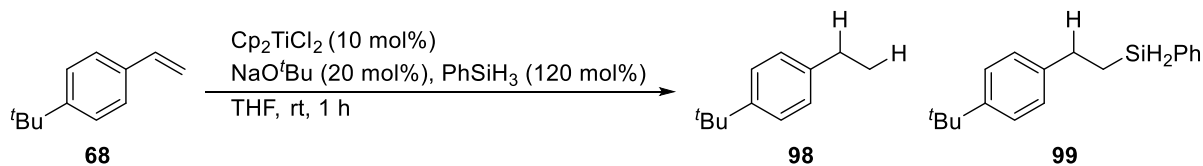
General procedure H was applied to titanium(IV) tetrachloride (4  $\mu$ L, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (2 mL). Approximately 61% of starting material was consumed, however the hydrogenation product **98** was observed in only a 4% yield by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. The rest was assumed to have polymerised under reaction conditions.

### Decreasing catalyst loading



General procedure H was applied to titanocene dichloride (4.4 mg,  $1.75 \times 10^{-2}$  mmol), sodium *tert*-butoxide (3.4 mg,  $3.5 \times 10^{-2}$  mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu$ L, 0.77 mmol) and THF (2 mL). No reaction took place.

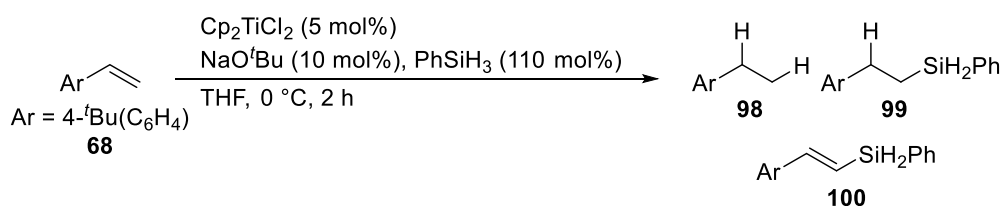
### Increasing catalyst loading



General procedure H was applied to titanocene dichloride (17.4 mg, 0.07 mmol), sodium *tert*-butoxide (13.4 mg, 0.14 mmol), 4-*tert*-butylstyrene **68** (0.13 mmol, 0.7 mmol), phenylsilane (0.12 mL, 0.84 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 45% yield and the hydrosilylation product **99** was observed in a 45% yield. The yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

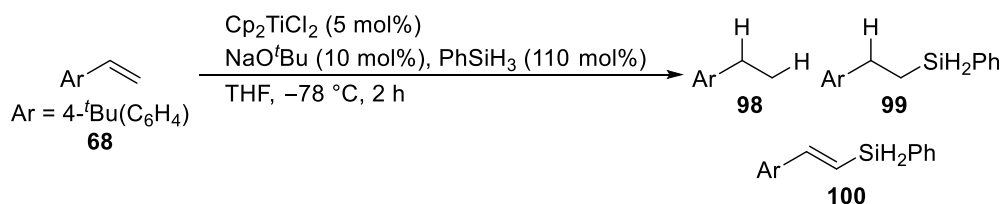
## Temperature variation reactions

### Reaction at 0 °C



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL) at 0 °C. The hydrogenation product **98** was observed in a 48% yield, the hydrosilylation product **99** was observed in a 36% yield and the dehydrogenative silylation product **100** was observed in an 8% yield. The yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

### Reaction at -78 °C

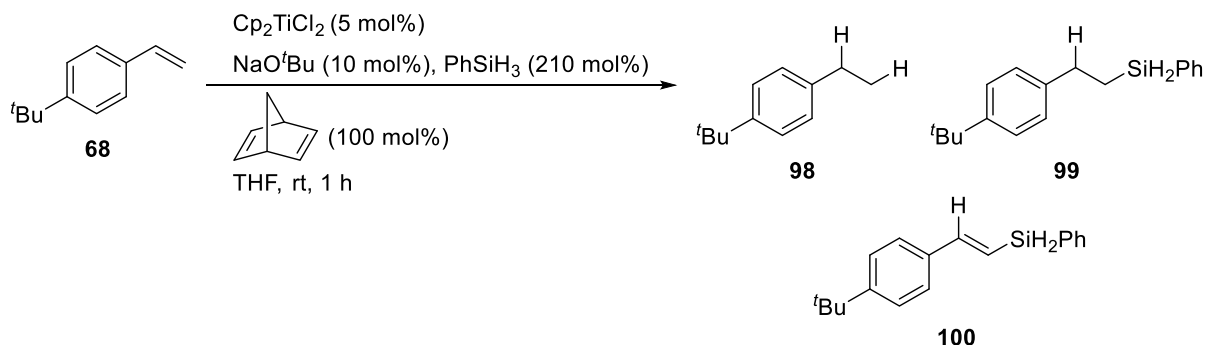


General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL) at -78 °C. The hydrogenation product **98** was observed in a 48% yield, the hydrosilylation product **99** was observed in a 44% yield and the dehydrogenative silylation product **100** was observed in an 10% yield. The yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>



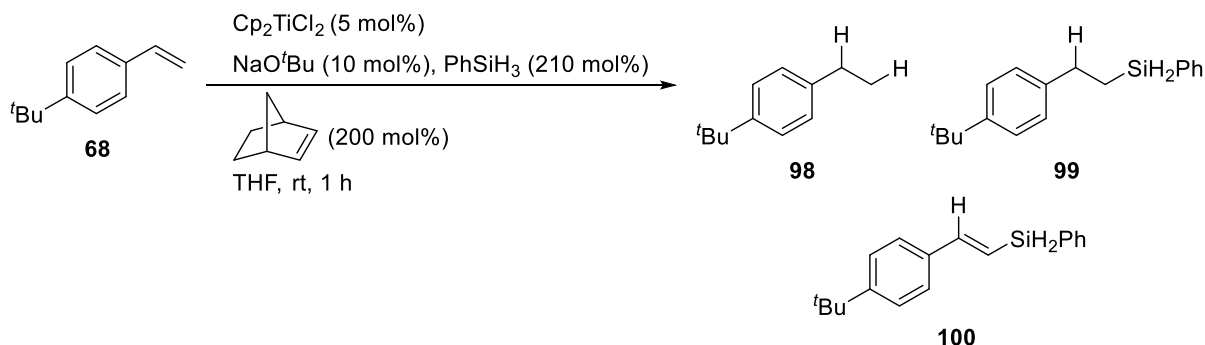
## Reactions with additives (Table 13, p. 59)

### Entry 1



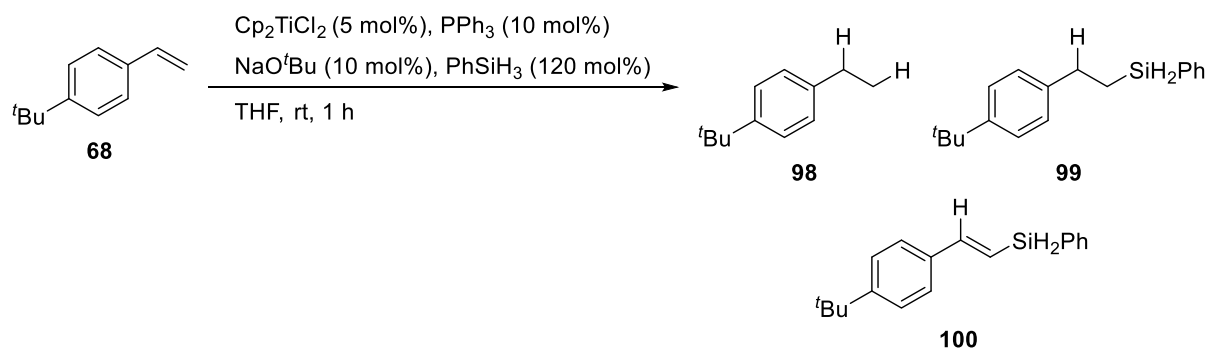
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), norbornadiene (71  $\mu\text{L}$ , 0.7 mmol), phenylsilane (0.18 mL, 1.47 mmol) and THF (2 mL). The hydrogenation product was observed in a 50% yield **98**, the hydrosilylation product **99** was observed in a 17% yield and the dehydrogenative silylation product **100** was observed in a 9% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>34,123</sup>

### Entry 2



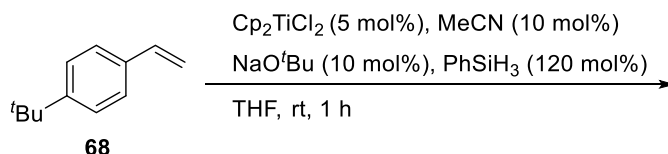
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.035 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), norbornene (132 mg, 1.4 mmol), phenylsilane (0.18 mL, 1.47 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 45% yield, the hydrosilylation product **99** was observed in a 42% yield and the dehydrogenative silylation product **100** was observed in a 10% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>34,123</sup>

### Entry 3



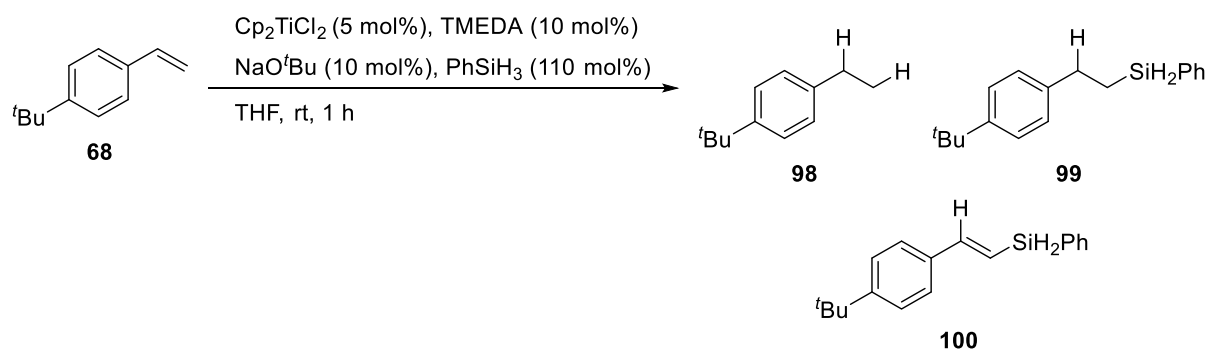
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), triphenylphosphine (18.4 mg, 0.07 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.1 mL, 0.84 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 41% yield, the hydrosilylation product **99** was observed in a 34% yield and the dehydrogenative silylation product **100** was observed in a 20% yield. All yields were determined by  $^1\text{H}$ NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data was consistent with literature values.<sup>34,123</sup>

### Entry 4



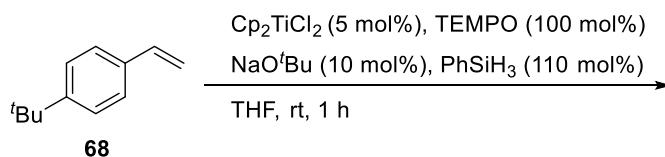
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), acetonitrile (3.7  $\mu\text{L}$ , 0.07 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.1 mL, 0.84 mmol) and THF (2 mL). No reaction took place.

### Entry 5



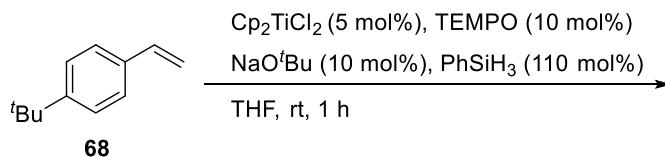
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), TMEDA (10.5  $\mu$ L, 0.07 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.1 mL, 0.84 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 47% yield, the hydrosilylation product **99** was observed in a 27% yield and the dehydrogenative silylation product **100** was observed in a 23% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

### Entry 6



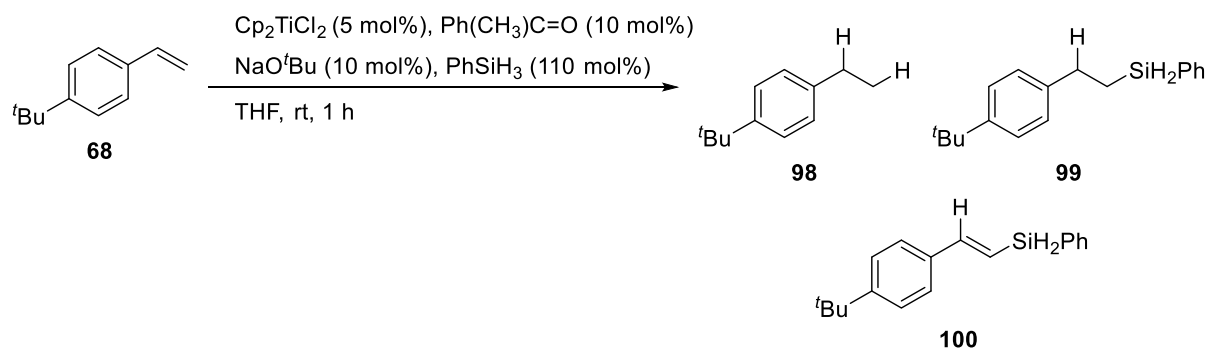
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), TEMPO (109 mg, 0.7 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.1 mL, 0.84 mmol) and THF (2 mL). No reaction took place.

### Entry 7



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), TEMPO (11 mg, 0.07 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (0.1 mL, 0.84 mmol) and THF (2 mL). No reaction took place.

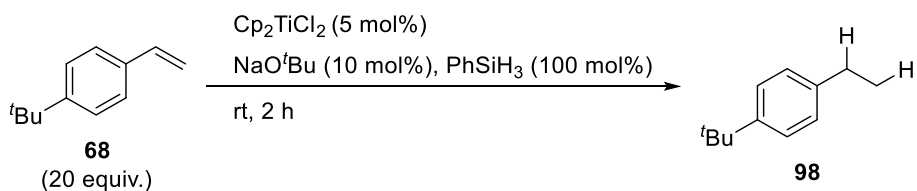
## Entry 8



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), acetophenone (82  $\mu\text{L}$ , 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). The hydrogenation product **98** was observed in a 50% yield, the hydrosilylation product **99** was observed in a 20% yield and the dehydrogenative silylation product **100** was observed in a 21% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

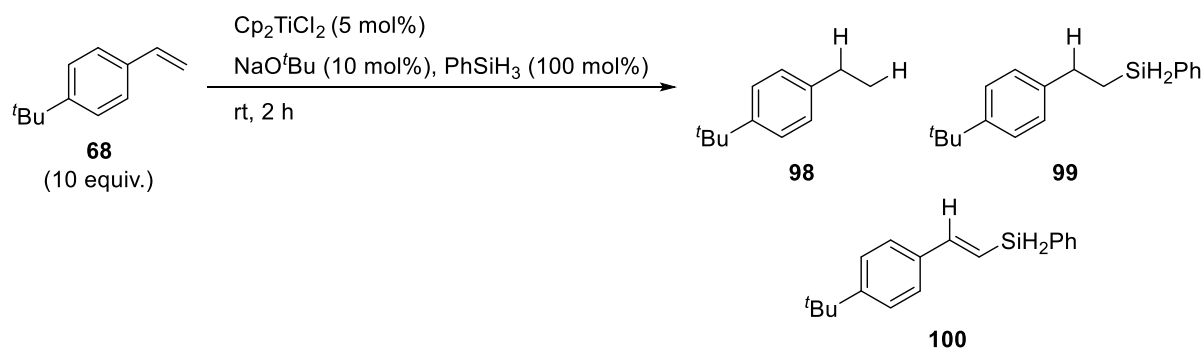
## Reactions in excess styrene

### 20 equivalents of styrene



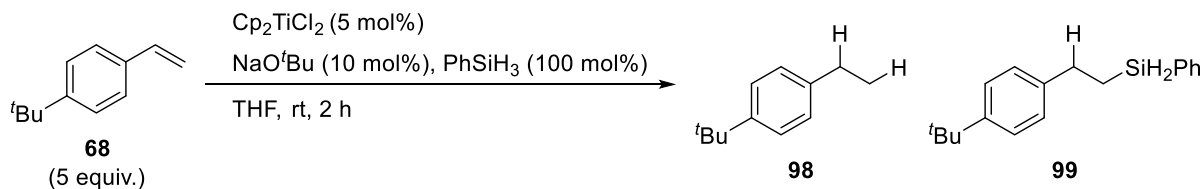
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (2.6 mL, 14 mmol) and phenylsilane (86  $\mu\text{L}$ , 0.7 mmol). Yield based on phenylsilane. The hydrogenation product **98** was observed in a 50% yield determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data consistent with literature values.<sup>123</sup>

### 10 equivalents of styrene



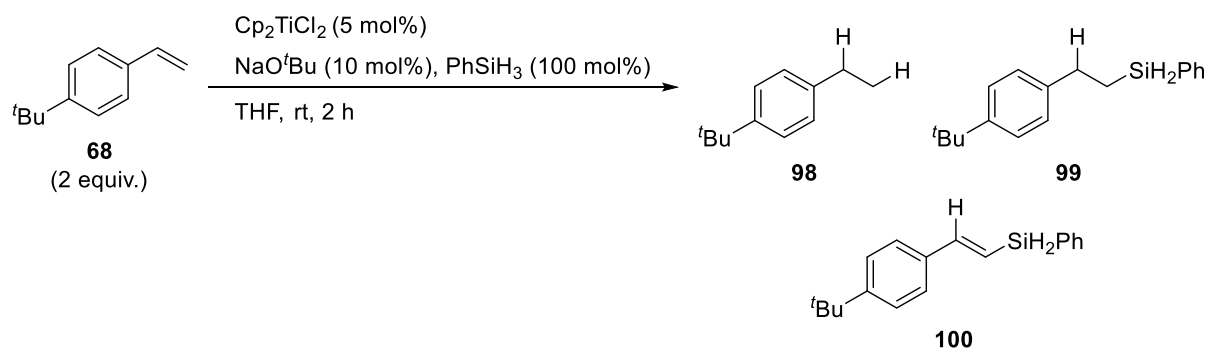
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (1.3 mL, 7 mmol) and phenylsilane (86  $\mu\text{L}$ , 0.7 mmol). Yield based on phenylsilane. The hydrogenation product **98** was observed in a 129% yield, the hydrosilylation product **99** was observed in a 7% yield and the dehydrogenative silylation product **100** was observed in a 67% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

### 5 equivalents of styrene



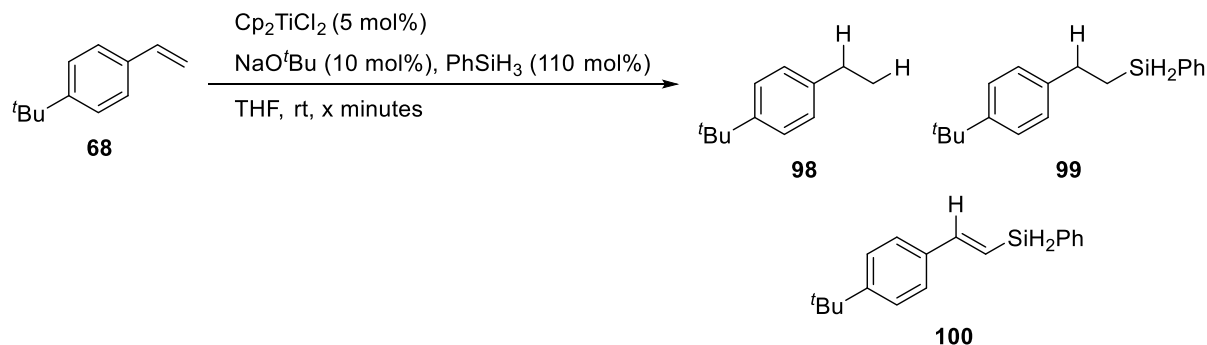
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.64 mL, 3.5 mmol), phenylsilane (86  $\mu\text{L}$ , 0.7 mmol) and THF (2 mL). Yield based on phenylsilane. The hydrogenation product **98** was observed in a 160% yield and the hydrosilylation product **99** was observed in a 20% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

## 2 equivalents of styrene



General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.26 mL, 1.4 mmol), phenylsilane (86  $\mu\text{L}$ , 0.7 mmol) and THF (2 mL). Yield based on phenylsilane. The hydrogenation product **98** was observed in a 90% yield, the hydrosilylation product **99** was observed in a 44% yield and the dehydrogenative silylation product **100** was observed in a 30% yield. All yields were determined by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. Data were consistent with literature values.<sup>34,123</sup>

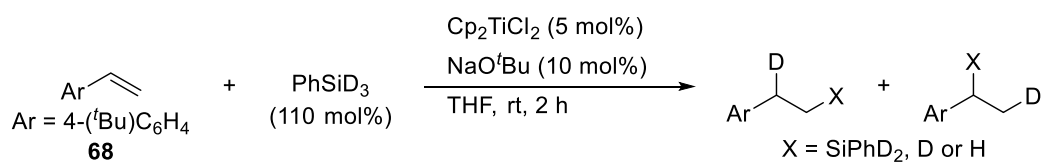
## Screening Reaction Time (Table 14, p. 61)



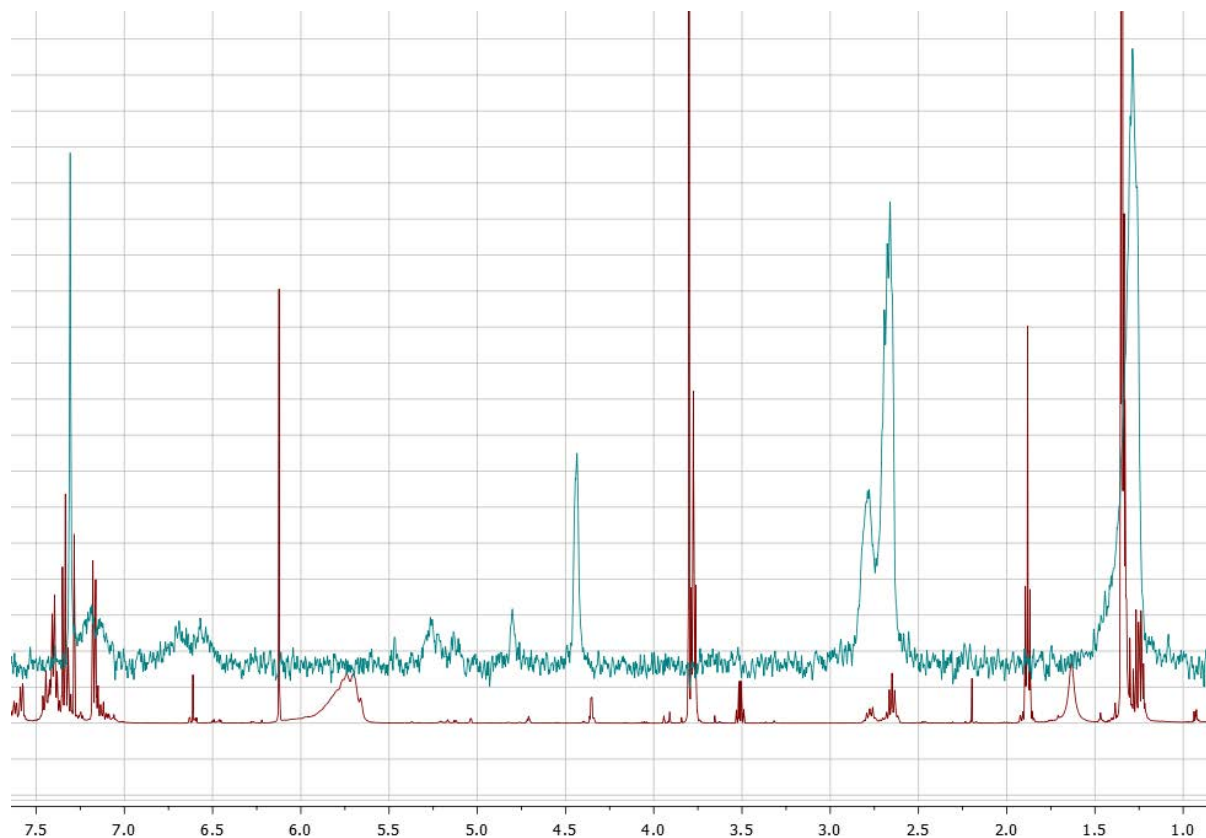
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), phenylsilane (95  $\mu\text{L}$ , 0.77 mmol) and THF (2 mL). A solution of 1,3,5-trimethoxybenzene (23.5 mg) in  $\text{Et}_2\text{O}$  (10 mL) was made up and split into ten different vials. An aliquot (~0.1 mL) from the reaction was then taken and injected into one of the vials at the indicated time intervals. Yields were calculated by  $^1\text{H}$  NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

## Deuterium experiments

### d<sub>3</sub>-Phenylsilane



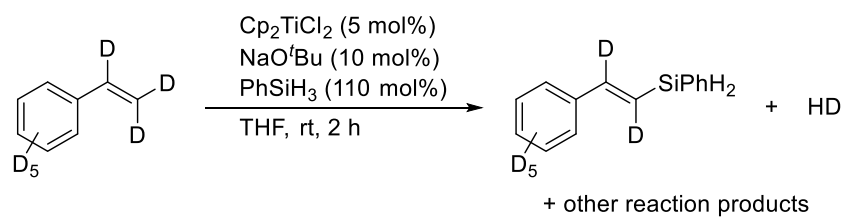
General procedure H was applied to titanocene dichloride (8.7 mg, 0.035 mmol), sodium *tert*-butoxide (6.7 mg, 0.07 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol), d<sub>3</sub>-phenylsilane (85.6 mg, 0.77 mmol) and THF (2 mL).



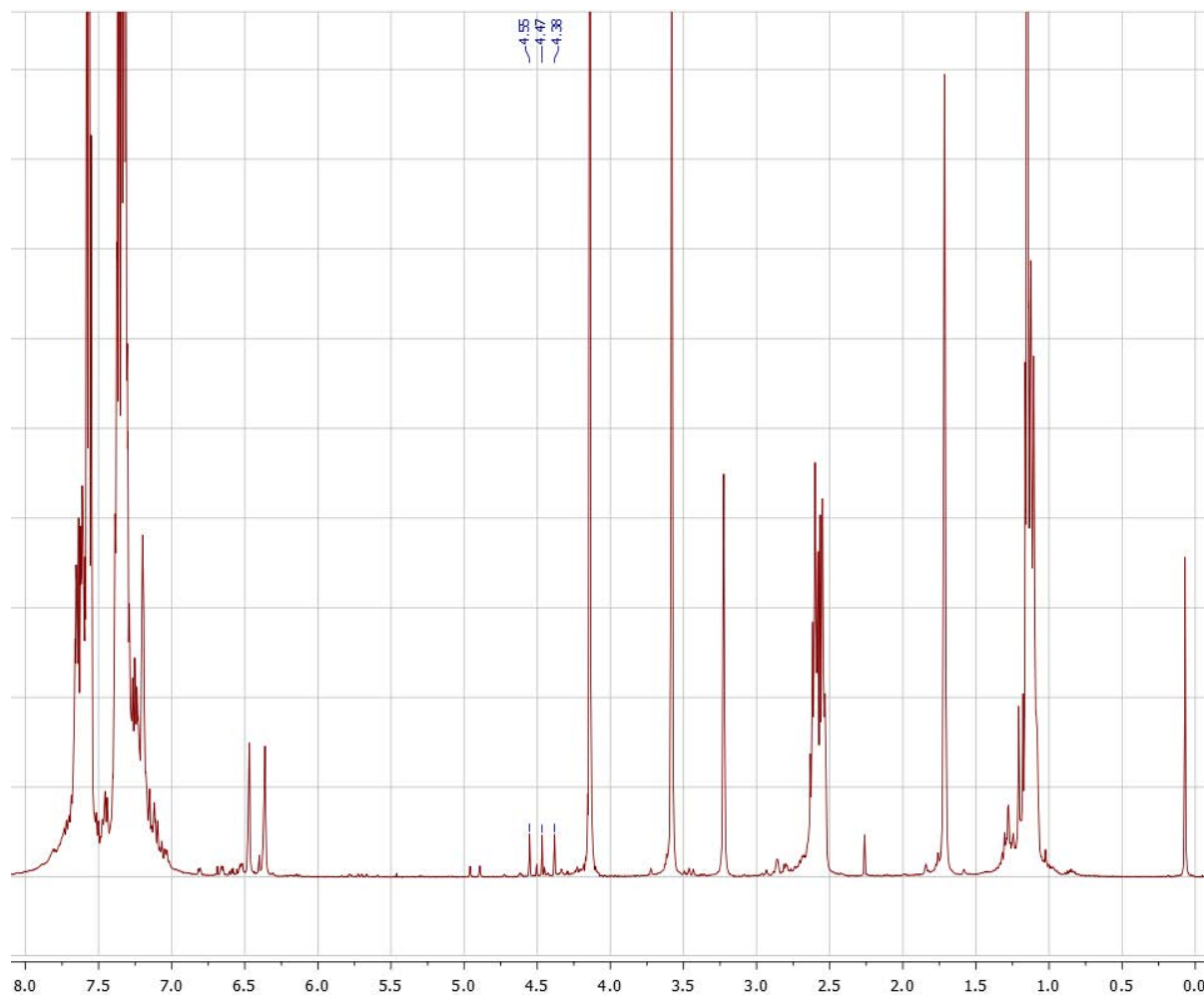
Red – <sup>1</sup>H NMR spectra. Cyan – <sup>2</sup>D NMR spectra.

Deuterium NMR indicates deuterium incorporation at benzylic (~2.75 ppm) and homo-benzylic (~1.3 ppm) positions.

## **d<sub>8</sub>-Styrene**



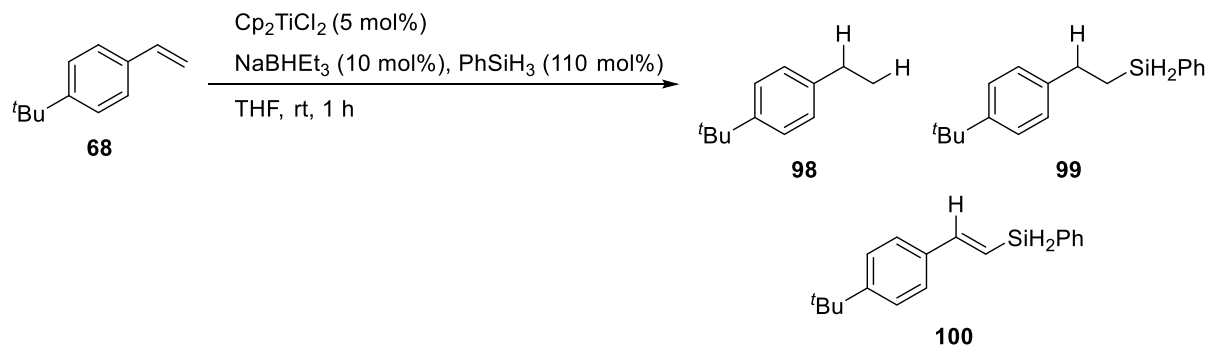
General procedure H was applied to titanocene dichloride (4.4 mg, 0.018 mmol), sodium *tert*-butoxide (3.4 mg, 0.035 mmol), d<sub>8</sub>-styrene (48 μL, 0.35 mmol), phenylsilane (48 μL, 0.385 mmol) and d<sub>8</sub>-THF (1 mL).



Peak at 4.47 ppm (H-D).

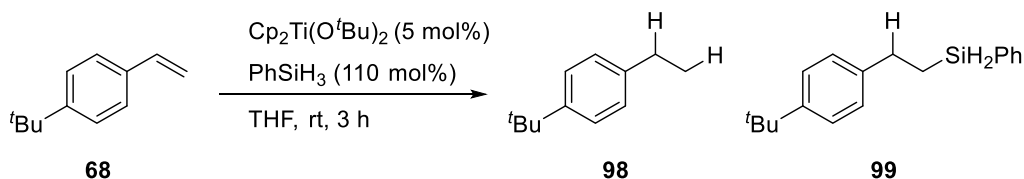


## Reaction with an organometallic hydride source



To a flask containing titanocene dichloride (8.7 mg, 0.035 mmol), sodium triethylborohydride (70  $\mu\text{L}$ , 0.07 mmol) was added followed by 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol) and the reaction mixture was diluted in THF (2 mL). Phenylsilane (86  $\mu\text{L}$ , 0.7 mmol) was then added and the reaction mixture was stirred for 1 hour. The reaction was then quenched with water (1 mL) and diethyl ether (3 mL) added in order to form two phases. 1,3,5-Trimethoxybenzene (23.5 mg, 0.14 mmol) was then added and the mixture stirred in order for it to dissolve and mix. An aliquot was then taken from the organic phase and the solvent blown off before being analysed by  $^1\text{H}$  NMR spectroscopy. The hydrogenation product **98** was observed in a 43% yield, the hydrosilylation product **99** was observed in a 36% yield and the dehydrogenative product **100** was observed in an 11% yield. Data was consistent with literature values.<sup>34,123</sup>

## Hydrosilylation using $\text{Cp}_2\text{Ti}(\text{O}^t\text{Bu})_2$ as catalyst



To titanocene di-*tert*-butoxide (11.4 mg, 0.035 mmol), 4-*tert*-butylstyrene **68** (0.13 mL, 0.7 mmol) was added followed by phenylsilane (95  $\mu\text{L}$ , 0.77 mmol). The reaction mixture was then diluted in THF (2 mL) and stirred for 3 hours. Reaction was then diluted with  $\text{Et}_2\text{O}$  (5 mL) and 1,3,5-trimethoxybenzene (23.5 mg, 0.14 mmol) added to the reaction mixture. An aliquot was taken from the reaction and the solvent removed before being analysed by  $^1\text{H}$  NMR spectroscopy. The hydrogenation product **98** was observed in a 47% yield and the hydrosilylation product **99** was observed in a 28% yield. Data were consistent with literature values.<sup>34,123</sup>

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